RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

VOL. 29 AUGUST, 1937 NO. 2

GROSS ANATOMIC CHANGES IN THE LUNGS[1]

By PHILIP HILLKOWITZ, M.D., *Denver, Colo.*

IN interpreting an x-ray plate the roentgenologist conceives in his mind's eye a picture of the actual condition of the organ or tissues, as translated from the shadow into a visual image on the retina. He is, or should be, therefore, familiar with the pathologic alterations underlying the structures under observation which necessarily implies some knowledge of the various morbid processes and their effects on the several organ systems and separate organs. We must bear with the pathologist in his pardonable assumption that pathologic anatomy and histology are the groundwork for scientific diagnosis and treatment of disease and should constitute an important part of the training of the internist, the surgeon, and particularly the roentgenologist. Yet, even the specialist in pathology is not often in a position to get a close view of diseased organs or tissues as they actually are in the living pulsating individual. When seen in the morgue at the autopsy table, or in the laboratory after operative removal, the picture is not quite like that seen by the surgeon *in vivo* when the circulation in the parts is still intact, and the colors and nuances of the structure are still alive. Much less true to reality is the appearance after immersion in preservatives and fixatives. Immeasurably distorted are the tissue cells when viewed under the microscope after undergoing the processes of fixation and differential staining with dyes. While we make our fine diagnosis by these valuable methods, the structures are not seen in their actual reality. However, like the archeologist or the geologist, we reconstruct from the altered material remains a good working image of what the organ or tissue would be like if observed under ideal conditions.

The task is far more difficult for the roentgenologist who has to base his interpretation on lights and shadows; yet, armed by his fundamental knowledge of the underlying lesion and the results of research of investigators in this field, he brings his talent to the service of the colleagues who consult him. His fund of experience will be greatly heightened when he personally follows his diagnoses through the surgery into the laboratory, and in the inevitably fatal cases to the morgue. The visual impressions thus gained are much more valuable than text-book illustrations, serviceable as those are, and will amply repay the time spent and greatly enhance his usefulness.

In the following sketches of the gross anatomy of the principal lesions of the lung, I shall endeavor to present only the high lights of the naked eye appearance with the hope that it will stimulate more detailed study in the special books and monographs on this comprehensive subject.

[1] Presented before the Radiological Society of North America at the Twenty-second Annual Meeting, at Cincinnati, Nov. 30–Dec. 4, 1936.

PNEUMONIA

In but few organs of the body is the contrast between the normal and the diseased so striking as in lobar pneumonia. Within a couple of days, the gray colored crepitant air-filled organ is converted into a red or reddish-gray solid and friable substance, to which has been given the classical term hepatization because of its resemblance to liver tissue. The consolidation is due to the outpouring of an exudate in the alveoli, displacing the air content, and filling the lumen with a fibrinous liquid which soon gels, giving the organ a solid consistence. On cutting into it, one finds a dry surface, with the fibrin plugs protruding from the bronchioles which lend the transected parts a granular appearance. The organ does not collapse when the thorax is opened and sinks when placed in water. It should be distinctly emphasized that despite its name the process does not necessarily involve the whole of the lobe or lobes but may affect only a portion. The extent of the involvement is due to several factors which for lack of space can only be mentioned here—the age of the individual, his resistance, and the virulence of the invading organism. The classification of pneumonia in its several stages of engorgement, red hepatization, gray hepatization, and resolution, so dear to the heart of the older writers of text-books, are not given their former prominence. We know now that some of these may be found at the same time in different portions of the lung due to the fact that the process is one of continuity, progressing from the hilus to the pleural surface.

In red hepatization the exudate in the alveoli contains many red blood cells which have escaped from the capillaries in the walls and give the organ the characteristic red or reddish-gray color. In the next stage, that of gray hepatization, the erythrocytes have disappeared, the capillaries in the septa are compressed by the exudate, and the color of the organ is distinct gray or grayish-yellow. In the stage of resolution there is a rapid liquefaction and absorption or discharge of the alveolar contents and correspondingly a return of the air into the sacs.

The distinction between lobar and lobular pneumonia is nowadays not given the prominence it once held. The pathologic process is practically the same, the extent of involvements as above mentioned varying with the virulence of the causative micro-organism and the age of the individual. The lobular or bronchopneumonia type is seen particularly in the young and the aged.

In rare cases, instead of resolution and a resorption of the exudate in the alveoli, there may be organization—the production fibrous tissue which fills the air sacs and shuts out the air. The process is known as a carnification of the lung.

In this connection, it may be well to describe lung abscess which may arise as a complication of pneumonia but more frequently of bronchogenic origin, due to the extension of a putrid bronchitis, the aspiration of a foreign substance, rupture of a cancer of the esophagus, etc. Here we have a destruction of the lung parenchyma, with formation of a creamy pus which may or may not be of foul odor, depending on the kind of infecting organisms.

It is interesting to note that lung abscess is seen three times more often in the right lung than in the left due to the more vertical course of the right bronchus. The abscess wall is ragged and tears easily. Sometimes in older cavities, it consists of a fibrous capsule.

In the similar lesion of gangrene of the lung, putrefactive processes are evident. The greenish or brownish softened tissue and dirty fluid emit an offensive odor. Large areas may be thus affected.

EMBOLISM AND INFARCTION OF THE LUNG

These unfortunate complications occurring after operative procedures, especially on the pelvic organs, and in chronic valvular disease of the heart, lead to an obstruction of the circulation in the affected part with the formation of a dark red

triangular area having its base on the pleural surface and the apex at the point of obstruction. The size of the necrosed area varies with the size of the nutrient vessel. In sudden death a large embolus may be found at the bifurcation of the pulmonary artery on one of the main branches. In the smaller vessels it may produce definite symptoms and certain characteristic shadows in the roentgenogram.

BRONCHIECTASIS

With the introduction of lipiodol into roentgenologic technic the diagnosis of this condition has been greatly facilitated. The bronchus may show a diffuse cylindrical or sac-like widening. The walls may be thinned out, producing hernial protrusions with accompanying atrophy or disappearance of the mucous membrane. On the other hand, there may be a thickening of the walls with hypertrophy of the mucosa and formation of polypoid elevations which may be mistaken for tumors. Some dilated bronchi may show alternating grooves and projections on the inner surfaces. The bronchiectases may ulcerate and form large cavities, particularly in tuberculosis.

ATELECTASIS

Of great interest to the roentgenologist is this condition in which the alveoli become airless. Leaving out of consideration the congenital type, we may consider the atelectasis due to compression as seen in empyema, pneumothorax, or serous effusion or pressure of a tumor, or enlargement of the heart. Another and frequent cause is obstruction of a bronchus by mucus or a foreign body. An extreme example of atelectasis is acute massive collapse of the lung. In all these cases the portion involved is airless, firm and retracted, and of a bluish or grayish color.

EMPHYSEMA

The opposite of the previous condition, emphysema, is manifested by an increased distention of the alveoli. The lungs are voluminous and cover the pericardial sac completely. Blebs project from the surface, and the margins are rounded. The lung pits on pressure and has a characteristic pillowy feel.

TUBERCULOSIS OF THE LUNG

The picture in this disease is one of great complexity. It differs greatly in accordance with the dose, *i.e.*, the number of bacilli invading the tissue and the resistance of the patient. It also varies as to whether the infection is primary or secondary. The former occurs in children who for the first time are attacked by the tubercle bacillus, and who, therefore, have not had the benefits of the immunizing process of previous minor invasions. Time does not permit a detailed exposition of the pathogenesis in tuberculosis, which is so essential to an understanding of the gross and microscopic lesions of this important malady. William Snow Miller's conception of the acinus as the unit of the lung which is discussed in this symposium also throws light on the pathology and is likewise illuminating in tuberculosis of the lung.

In the primary tuberculosis of childhood there are one or more caseous areas of greater or lesser extent—in effect, patches of tuberculous bronchopneumonia, also miliary nodules in the vicinity. Characteristic of the primary origin is the presence of chains of minute nodules along the lymphatics leading to the regional lymph nodes which are markedly enlarged and caseous.

In secondary tuberculous infection of the lung, by far the most frequent, we have a great variety of gross lesions which it is difficult to classify satisfactorily. According to Boyd, we may, as a matter of convenience, divide the cases into the fibrocaseous type, caseous pneumonia, and acute miliary tuberculosis. In fibrocaseous or ulcerative tuberculosis of the lung we may see one or several cavities, usually situated near the apex. They have rather smooth, thickened fibrous walls; occasionally an intact bronchus or

blood vessel may wend its way across the cavity. In the adjoining tissue and more or less distant areas are opaque solid lesions of gray color and of varying size, down to minute miliary lesions in the lower portion. There are, of course, infinite gradations of this gross pathologic picture, depending on the play of contending forces, of the size of the dose of tubercle bacilli *versus* the resistance of the individual. Here the roentgenologist has been of immense assistance to the clinician in interpreting the shadows on his plate in terms of pathologic anatomy. The acinar unit, as it is invaded by the tubercle bacillus with the involvement of the respiratory bronchiole by granulation tissue, the exudate, pouring into the alveolus or its collapse by inflammation of the septa, constitute a key to the explanation of the gross appearance as seen in reality or on the shadow. The white strands on the cut surface, the thickening of the bronchi of the blood vessels and of the pleura are indications of fibrosis, the conservative productive process.

In tuberculous caseous pneumonia, we see a large portion or all of a lobe or even of the entire lung converted into a solid mass, not unlike the appearance of gray hepatization in pneumonia. It may also be mistaken for a primary carcinoma of the lung. The lymph nodes are likewise apt to be involved in the caseous process.

In the acute miliary type, the lungs are studded with miliary tubercles more or less translucent, the later lesions being opaque and caseous.

Syphilis need only be mentioned by name as its occurrence is rare and difficult of differentiation from tuberculosis. Hodgkin's disease, also quite rare, is alluded to because of a case seen in consultation with Dr. Wasson, in which cavities were present and the diagnosis was made only by microscopic examination.

TUMORS OF THE LUNG

In the last decade or two primary carcinoma of the lung has assumed a marked importance. Formerly considered a rarity, it now ranks second only to carcinoma of the stomach. Whether the greater incidence is due to better methods of diagnosis or to an actual increase is beside the point. The roentgenologist should always keep the possibility in mind. Benign neoplasms are rare in comparison with the malignant, usually carcinoma. Growths resembling round-cell sarcoma, and so diagnosed, have been found on closer investigation to be of epithelial origin.

The great majority of primary carcinomas of the lung (90 per cent) constitute the so-called hilus type which originates in the bronchus from whence it spreads through the bronchial tree into the surrounding lung substance, producing a gray mass often enlarged in size by the involvement of the neighboring lymph nodes. The growth is usually firm but occasionally undergoes necrosis and may be the seat of abscess or cavity formation. By pressure on a bronchus it may cause atelectasis of a portion of the lung or a bronchiectasis.

In a small proportion the tumors are of minute size, just palpable to the finger and resembling miliary tuberculosis. There is still a rare diffuse form of primary carcinoma of the lung involving a whole lobe, which may be mistaken for a pneumonia.

DISCUSSION

DR. PHILIP HILLKOWITZ (closing): I have little to add except to say that we were greatly stimulated by Dr. Dunham's challenge to the pathologists and physiologists to clear up a great many points that we do not know.

It has always been a great pleasure to have our colleagues in the roentgenological field come to the pathologists and stimulate us by these perplexing questions. It is always productive of progress.

CRANIAL DYSPLASIAS OF PITUITARY ORIGIN[1]

By HECTOR MORTIMER, GEORGE LEVENE, *and* ALLAN WINTER ROWE*

From the Department of Biochemistry, McGill University, Montreal, Canada, and the Evans Memorial for Clinical Research and Neuro-endocrine Research, Boston

PART I

OUR interest in the proportions and architectural structure of the human skull, as seen in cranial skiagrams, dates from the observation by the senior author, in 1932, of changes suggestive of such as are known to occur in acromegaly, in a male of 26 years—the subject of catatonic dementia præcox.

When first seen, this patient had been about a year in Worcester State Hospital and had been studied for over seven months by the research service (1). In view of this finding, certain facts in the patient's history were of special interest.

Described as normal at birth, he walked at one year, but at the age of three he showed a "weakness of the legs" and was unable to walk for several months. At eight or nine he suffered from leg pains, described at the time as "growing pains." There was a history of trauma to the face by a baseball bat at the age of twelve, to which was subsequently attributed the frequent frontal headaches of which he later complained, as well as the nasal septum deviation for which he underwent an operation when 18 years old.

When about fourteen or fifteen years old he grew rapidly so that, from being a boy of average size in public school, he found himself, when he entered high school, to be one of the tallest boys, not only in his class, but in the school.

In public school his scholastic record had been good, but in high school he failed markedly in performance and, since he was ambitious, this was one of the earliest causes of his self-dissatisfaction. While in high school he suffered greatly from fatigue and frequently complained of headache, vertigo, and occasionally of diplopia.

When examined at the age of 26, in 1932, he showed no evidence of any organic disease, but the data derived from the first month's intensive physiological study showed deviations from normal limits highly suggestive of disturbed pituitary function (2). The second month's study, carried out after an interval of two months, gave the data which, while not within normal limits, did not point so strongly to pituitary implication; and a final month's study, done after a further intermission of two months, gave data which materially were within low normal limits.

The patient's psychiatric state during these three periods also showed variation. During the first he was in well marked catatonia; during the second he was "reacting" and excitement was dominant, while during the third he "recovered" to the extent that he could usefully be employed in clerical work in the hospital office.

Assuming for the purpose of further investigation that the changes in physiologic function levels were not primarily of psychogenic origin, but might be related to disturbance of pituitary function, it became a matter of great clinical interest to see whether he bore any stigmata of past growth disturbance, either of under- or over-active nature.

His height was 181.6 cm., trunk height 95.7 cm., so that his sitting height index was 0.526; his span was 67 mm. greater than his height—proportions which are by no means abnormal, despite the burst of growth reported in the history. When

[1] A preliminary report on this material was made at the annual meeting of the Association for the Study of Internal Secretions, at Milwaukee, June 12, 1933.

* Deceased Dec. 6, 1934.

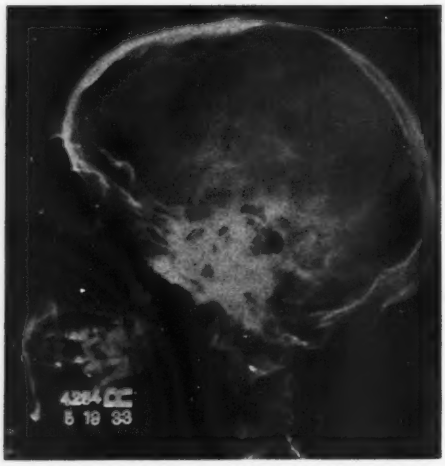

Fig. 1. Patient, F. G., aged 26 years, male, No. 4,254, Worcester State Hospital. Diagnosis: Catatonic dementia præcox.

viewing this patient naked, however, one was struck by the fact that, while the extremities were heavy in both bone and musculature, the thorax was poorly developed and poorly clad. There was well marked dorsal kyphosis, the chin was prominent and held high, the forehead seemed receding with prominent supra-orbital ridges, and the body was held in a slouch with flexion of the knees, slight genu valgum, and eversion of the feet, which were slightly flat—the whole presented a picture not unlike the posture in some acromegalics.

The cranial skiagram (Fig. 1) is of particular interest. The whole calvaria is thick, particularly in the frontal bone, the inner table of which is thicker and denser than normal, a sclerosing process apparently having extended from the inner table into the adjacent middle table, which seems to have undergone earlier some degree of "expansion."

The prominence of the supra-orbital ridges here seems to be related to the development of the frontal sinuses which, while not extensive vertically, are large in their lateral and anteroposterior diameters. The maxillary antra are large, as are the mastoid air cells. The whole face is well pneumatized and there is a slight degree of prognathism, which is somewhat greater than is shown in the skiagram owing to part of the film having been cut off anteriorly. There is well marked synostosis of the coronal suture, which, in view of the patient's age, cannot be regarded as entirely normal. The sella turcica is normal.

A general clinical impression at that time seemed to warrant the provisional description of such a cranium as "sub-acromegalic," and we felt inclined to the view that during adolescence this patient had had a transitory hyperpituitarism which had manifested itself in his general body conformation as well as in his cranial proportions and structure.

At this stage it occurred to us that the recognition of such conditions might possibly serve as a "lead" to a wider concept of the main problem under study. Here was a psychotic patient, apparently free of organic disease, in whom there was some evidence of disturbed pituitary function, indicated by data acquired from objective physiological tests carried out over a period of seven months. This disturbance had been most profound when the psychosis was deepest, and as the findings approached normality the patient passed through a stage of psychiatric improvement, to relative recovery of sanity. Also, with a definite history of an emotional and mental change in the second decade of life, he had in that same decade as the result of his various growth processes acquired a bodily conformation which could not be regarded as "normal" in that it did suggest a definite, though slight, degree of acromegaly. Furthermore, stigmata of such processes in the past were recognizable in the cranial skiagram.

As a hypothesis it might reasonably be argued that his psychiatric condition might owe its fundamental etiology, perhaps in part, to abnormal functioning of those factors which regulate and control growth and development in the widest sense, in which must be included, not only bone and muscle, but also the central nervous system whose most highly evolved function,

as well as that of most recent acquisition in phylogeny, is "mind." It is obvious that for the purpose of investigation a standpoint had been assumed which favored the physiogenic rather than the psychogenic etiology of mental disease.

The first step in the utilization of this lead was a scrutiny of the cranial skiagrams of all patients previously studied by the research service. At that time between 60 and 70 males, between the ages of 20 and 40 years, had been fully investigated under Hoskins' "seven-month plan" (3). All had had cranial skiagrams taken and these were examined by the senior author with Dr. Hoskins and Dr. Sleeper, the identity of the patients not being known. Of this number, 11 were found to show definite hyperostosis and hyperpneumatization, allowing them to be grouped with the original case. The significance of the changes seen in these crania became evident when they were compared with the skiagram of a female patient, not studied in the research service, an acromegalic twice operated upon by Dr. Cushing for eosinophilic adenoma of the pituitary, who since had become demented. At the time of the second operation the hospital case-notes contained a statement that the thickness of the skull at the vertex was 15 mm. The 11 cases found showed changes similar in type, though less in degree, to the changes evident in this known acromegalic, with the exception that none of the 11 showed any abnormality of the sella turcica.

Since these skiagrams had been taken to ascertain the condition of the sella, it became evident that there had been a tendency to report on the condition of this structure, omitting to observe the general cranial change, or to have accounted for it, if seen, by the fact that there is considerable normal variation in human crania. It was evident that, clinically at least, there was a tendency to focus disproportionate attention on variations of size and shape of the sella, as indices of pituitary function. In other words, observers tended to fail to see the "forest" of evidence of general and differential cranial change for the "trees" of the sella turcica. We had subsequently cause to regret this fact, when it was found, in certain cases of special interest studied in the past, that only a circumscribed sellar skiagram had been taken, from which little information could be derived beyond the fact that the pituitary fossa was normal in size and had not undergone structural change.

Naturally it was recognized that there is considerable variation in developmental proportion and architectural structure in human crania and that there may be many influences responsible for this. Apart from the effects of disease, congenital or acquired, local or general, it is usually admitted that race and family, sex and age, nurture and nourishment are important factors, whatever may be the mechanisms by which they act.

It did appear reasonable, however, that a radiologist, routinely inspecting a large number of cranial skiagrams from any given population, even though composed of mixed racial elements, would in the course of the observation become impressed, consciously or unconsciously, with the degree of average variation, beyond which at either extreme he would have little difficulty in recognizing degrees of abnormality, although he might be unable to suggest a causal mechanism. Also such observations would not be of lessened value just because the zone of average cranial growth, in the population, had not been delimited by recorded measurements derived from roentgenologic studies.

This point of view was discussed with several roentgenologists of wide experience who found themselves in agreement with it. The skiagrams of the 11 cases from Worcester State Hospital were next examined by one of us (G. L.), who compared them with skiagrams of acromegalics, previously studied in that institution, and his opinion was that none of the crania was normal. All showed changes similar to those seen in the diagnosed acromegalics: one to a "slight" degree; four "moderate" in degree, and

in six cases to a "well marked" extent. At this point it may be of interest to note that on June 8, 1932, when Dr. A. W. Rowe reviewed the data on 32 cases, studied under the "seven-month plan" (3) at Worcester State Hospital, for the purpose of endocrine diagnosis, six of these 11 cases were included, unknown to Dr. Rowe. Five of them he diagnosed as "pituitary dysfunction" and in the sixth he suggested the possibility of this condition as a factor in the case. Four of the cases showed abnormal growth of body hair, in two restricted to the sacral region, and in another it was so generalized and abundant as to give the patient a pithecoid appearance. One patient was tall and described as "eunuchoid," while another, aged 16, was 179.5 cm. in height, with a sitting height index of 0.511 and a history of rapid growth in the previous two years. His frame was powerful, with very large hands and feet. There was marked dorsal kyphosis and lumbar lordosis. The ears were "very large" and the lips "prominent and thick." The lower jaw was heavy and the general appearance suggested acromegaly.

It was, of course, obvious that a series of 11 cases was inadequate to indicate the possible frequency with which a dyspituitarism in the adult, recognizable physiologically, might correlate with an earlier dyspituitarism during the growth period, whose imprint on cranial form and structure would remain for subsequent recognition in the cranial skiagram.

While it might seem more reasonable to suppose that adult dyspituitarism would be most likely to occur in those whose glandular function during growth had been unstable, the possibility of the condition developing in cases in which the growth period had been uneventful had to be admitted. Nor could it be inferred from such a series whether or not a general disturbance of the endocrine control of somatic growth might be a fundamental factor in the later production of mental disability.

The problem seemed to formulate itself as three questions:

(1) What is the frequency of occurrence, in a significantly large group of adults who are free of organic disease, of such individual variance from average cranial form and structure that the skull can be regarded as dysplastic?

(2) If, on the evidence already existing, the assumption is made that the pituitary gland plays a dominant rôle in the matter of cranial form and structure, what proportion of individuals manifesting cranial dysplasia can be shown independently to offer other evidence of pituitary disability?

(3) What is the frequency of occurrence of mental disability or disease in individuals who show both cranial dysplasia and physiological evidence of disturbed pituitary function?

In order to carry out the investigations necessary to answer these questions, it was decided to continue the inquiry at the Evans Memorial Hospital, in Boston, where for many years Rowe (4) and his co-workers had been engaged in studying the physiologic data acquired from a large series of patients referred for endocrine diagnosis, and had in use a diagnostic method based on a preliminary comprehensive general medical examination of the patient, amplified by a large series of objective tests by which the individual's physiologic function level could be estimated.

There were then on file very complete records of 4,000 cases studied by this method, which included lateral and postero-anterior cranial skiagrams of 3,000 of them, all of which had already been "read" by one of us (G. L.) and his opinion recorded. This group included both sexes, children and adolescents as well as adults. The fact that such a group constitutes a special or selected population has certain advantages, which outweigh the inherent disadvantage that figures so derived are probably not applicable to either an ordinary healthy population or even to a general hospital population.

The advantages lie in the quite ade-

quate number of cases, as well as the fullness of the studies already done, and the accessibility of the data. Of the first 1,000 patients studied, all of whom had been referred as possible endocrine cases, 40 per cent had been shown not to be endocrine and these would serve usefully as control material in checking findings. It was also an advantage that organic diseases, which might add a complicating factor, could largely be excluded; and the cases were referred from such a wide area and the various racial stocks were sufficiently present to provide a representative American population. But the chief advantage lay in the fact that whether or not, in the case of any individual, an endocrine factor could be demonstrated, at least he was "known" physiologically as to the degree of his normality or abnormality, which fact might subsequently aid in the evaluation of the possible significance of any such single datum as might have been found in the cranial skiagram.

The general plan of the investigation was to study all cranial skiagrams on file in the institution, without the identity or diagnosis of the case being disclosed to the examiners, who selected all those which seemed definitely to be dysplastic, stating the facts on which they based their opinion. The final diagnosis on record after one or more periods of physiological study was then added to the list of the dysplastic cases. This method seemed to be reasonably secure in its objectivity.

It was felt that, from the clinical craniological viewpoint, postero-anterior and lateral cranial skiagrams should be as informative and as valid as projection or orthodiagraphic drawings of dried crania, on which to form an estimate of the differential growth record, beside giving an accurate impression of density and of architectural structure, whether normal or pathological. We were, of course, aware that distortions did arise due to radiographic technic, but a preliminary study of dried crania, which were measured both by micrometer calipers and on the skiagrams, made with a standard technic, convinced us that these would not really invalidate this method of study.

There is, however, at first a twofold disadvantage in the use of the cranial skiagram for this purpose. Craniologists have not as a rule used x-rays in the examination of their material, so that there are certain omissions in observation of structure, and the radiographic changes concomitant to the conditions they describe have to be inferred. Also, in such an informative disease as acromegaly, much of the authoritative work on the changes produced in the skull had been done before current use was made of the skiagram as a diagnostic agent, so that accurate description of early change or change of slight degree is lacking. Full description had to await postmortem examination, by which time the disease had as a rule existed many years, with the possibility of factors either secondary to the pituitary condition, or even relatively unconnected with it, markedly altering the final picture.

Since our interest in cranial dysplasia had arisen from the "subacromegalic" type, our first attention was directed to the consideration of all the varying effects which acromegaly may produce on the cranium, both in its proportions and in its structure.

THE CRANIAL CHANGES IN ACROMEGALY

For a full appreciation of the possible variety of changes which the acromegalic process may produce in the human skull, we thought it desirable to review the findings recorded, from the first recognition of the condition as a syndrome associated with pituitary tumor by Marie, onwards, as cases were reported in the world literature. It should be borne in mind that although the later summarized descriptions of the pathological findings are more authoritative, being backed by a greater number of cases, they in no way contradict or diminish the value of the earlier observations as *findings*, although disagreement may arise with the interpretation put upon the findings, in offering

explanation of the mechanism of production of the deformities noted during life.

Marie (6) described the cranial changes seen in his cases as follows:

"The cranium is but little altered in shape and size, or at least its alterations are not obvious. The forehead is usually rather low, with a very marked prominence of the orbital arches (due especially to the dilatation of the frontal sinuses). . . . The cheek bones rather prominent and bulky (not from hypertrophy of the malar bone, but from dilatation of the maxillary sinuses); . . . this prominence is in part masked by the elongation of the face. The chin projects markedly forward and downward; it is large and massive; moreover, the lower jaw is altogether considerably increased in size, and as the upper jaw does not undergo the same modifications, a very marked degree of prognathism often ensues. The teeth undergo no modification in size, but in consequence of the enlargement of the lower jaw they are here seen to be separated a little from one another. . . . The bones of the cranium and face are the seat of a more uniformly distributed hyperostosis (or rather the increase in size is due much more to the dilatation of the frontal sinuses than to a true hyperostosis), without the formation of osseous tumors or definitely circumscribed bosses. . . . The results of the examination of the skeleton of my patient by my friend Dr. Auguste Broca (7) have shown us that it is especially the spongy tissue which is the seat of the hypertrophic processes."

As the syndrome received increasing attention and fresh cases were reported—Souza-Leite (8) had collected 38 cases in 1890—it became evident that the skull might not always undergo the classical deformity. Marie also had recognized less well-marked cases, which he called "formes frustes," as well as a variety in which the lower jaw is not enlarged—and might even appear small in comparison with the upper jaw—which he called the square variety ("type carrée") in contrast to the classical "ovoid" appearance of the face (9). Similar observations had been made by others (10, 11, and 12).

In 1897, Sternberg, the Viennese pathologist, published his monograph (9) on acromegaly, collecting data from 210 cases in the literature at that time. In summarizing the pathological changes in the osseous system as they affect the skull, he points out that there have been cases in which the brain itself has been enlarged as a whole (13 and 14), calling for an increased cranial capacity and hence enlargement of the skull. But apart from this, the skull is frequently enlarged, coarse, and heavy, with thick walls, especially if the disease has lasted a long time. Its circumference may or may not be increased. Muscular attachments are apt to be overgrown and prominent, especially the external occipital protuberance, the mastoid processes, and the styloid processes of the temporal bones.

Small exostoses may occur on the wall of the aqueductus vestibuli and, more rarely, on the upper surface of the sphenoid bone. There may be deformity of the clinoid processes, and the sella turcica may be widened in all directions, *or, on the other hand, it may be normal.* The vascular channels on the inner surface of the skull are deepened, and the arterial and venous foramina enlarged.

The air sinuses are enlarged, although not all to the same extent. The frontal sinus extends higher up into the diploe of the bone, so that the usual saw-cut, in the horizontal plane of the skull, 1 cm. above the orbital curve, opens into the sinus. If the expansion of this sinus is marked, even although the anterior wall is thin, it may markedly alter the shape of the forehead, a deformity which may be increased, in other cases, by hypertrophy of the bone. A similar condition may be found in the mastoid cells and maxillary antra as well as in the ethmoid capsule. Bulging of sinus walls may cause neighborhood deformity; the orbit may be narrowed by expansion of ethmoid cells, of the lower wall of the frontal sinus, or of the upper wall of the maxillary antrum. Such expanded sinus walls may be paper thin, or, on the other hand, they may be thick, a change which he attributed to long duration of the disease. The maxillary alveolar process may be hypertrophic, and still more so the body and rami of the mandible, and the conditions of prognathism, alveolar prognathism, or progeniacism thus produced (15). Sternberg used the word "prognathism" in its correct

anthropological sense of projection of the masticatory framework in front of the forehead, when the skull is orientated in the Frankfurt plane. He disapproved of the use of the word by contemporary French writers to describe the condition in which the teeth of the lower jaw project beyond those of the upper, and prefers to use for this latter condition the more correct term suggested by Ludwig Meyer in 1868 (16), who grouped skulls, showing this deformity from a variety of conditions, under the title "Crania progenea"[2] or, in colloquial German, "progenee Schädel."

Amongst more recent English writers there has been a tendency to use the Latin adjective as an English noun (17). The original derivation is from the Greek προγένειος, *prominent chin*, *progeneum* being the permissible latinization. In English, the noun from this would be "progeneity" or "progeneism" and the adjective "progeneic"; all are awkward terms. Better words can be got in English by direct derivation from the Greek—"progeniac" the adjective, and "progeniacism" the noun, both of which aptly express the anatomical condition in regard to which they are most applicable.[3]

Sternberg also notes the "sclerotic hypertrophy" of the vault of the skull described by Thomson (18), and draws attention to the changes arising "from the marrow of the bones, especially those in which, during growth, the marrow remains preserved," quoting Duchesnau's case (19), of which the skull is an example, in which resorption may predominate and even be extreme. He pointed out that, in general, the medullary spaces between the osseous septa are enlarged, but that these latter may themselves be hypertrophied. Thus, depending on whether the periosteal or myelological changes predominate, the compact bone may be thickened at the expense of the cancellous part, or the cancellous may be very vascular and over-developed, with the compact bone extremely thin (20).

Finally, it is clear that Sternberg considered the cranial changes to be the result of the primary changes in the jaws. He says:

"The strong formation of the masticatory apparatus demands powerful points of compensation in the head. These come about either by thickening of the solid or through dilatation of the hollow supports, or through distribution of the weight over a large surface. To the first the hypertrophic zygomatic arch corresponds; to the second the dilatation of the air sinuses, and the increase of the skull to the third. All changes in the form of the skull thus stand in causal connection."

In 1911, Keith (21), dissatisfied with "the empiricism of craniological methods" and aware of the necessity of "applying more rational principles to the elucidation of the problems of head form," sought in the study of acromegalic crania "a clue to some of the circumstances which determine the shape of the head and face." At that time he estimated that there were records of some 400 cases of acromegaly, "yet nowhere was there to be found an exact inquiry into the nature of the growth changes of the skeleton, particularly of the skull."

Keith had access to some twelve acromegalic crania, all of which he studied, and from a detailed analysis of six of them he made good the lack on which he had commented, by a classic study, which not only demonstrated the nature and significance of the acromegalic changes, but justified his conclusion that these changes, essentially of the nature of true growth, were similar to those conditions that normally are to

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[2] In a footnote on page 96 of the paper cited (16) and in a note on page 336, Meyer says: "It is not easy to find a convenient term for this form of skull. On the advice of Professor Sauppe, I selected one part (the chin) instead of the whole lower jaw, for the construction of a name which would bring out the characteristic appearance, while being academically correct. In Greek γένειον is *the chin*, and προγένειος means *prominent chin*, hence Crania progenea, progenee Schädel."

[3] We are indebted to William Dudley Woodhead, Professor of Classics in McGill University, for drawing our attention to the following excellent description of this deformity by Theocritus:

ἦ δά γέ τοι σιμος καταφαίνομαι ἐγγύθεν ἦμεν; νύμφα, και προγένειος; ἀπαγξασθαί ποησεῖς.

"At close quarters, Maiden, do I appear to you to be snub-nosed and long-chinned? You will make me hang myself!" (*Third Idyll*, ΚΩΜΟΣ, *line 9.*)

be found in anthropoid and neanderthaloid crania, and which he suggested are due to probable hyperpituitarism.

He thought the evidence that there might be an actual increase in cranial capacity was inconclusive. Taking the normal adult male calvarial thickness as varying from 5 mm. to 7 mm. and quoting Beadles (22) to the effect that a thickness over 12 mm. was to be regarded as pathological, he found that, in the vault of the skull, the frontal region was the part first and most affected. In six cases the frontal bones varied from 6 mm. to 15 mm., a range which was also found in the parietal region. The change affected only that part of the calvaria bounded by the temporal lines on each side, so that a "sagittal bar" of thickened bone was formed, which rested in front on the supra-orbital bar, and behind on the external occipital protuberance. He considered this change comparable to the growth of the sagittal crest in the gorilla, the function of which was to act as a "fulcrum of origin" for the temporal muscles. This formation could be "correlated to the masticatory changes" in the acromegalic.

A point of great importance was that the calvaria also varied in structure. In two cases the bones of the vault were thickened and porous, as in osteitis deformans: two showed thickening but with the inner and outer tables retained; while in the remaining two the bones were of normal thickness but were increased in density. In all six the inner table of the frontal bone especially above the orbital plates, showed the tendency to the formation of small dense osteomas, and a similar condition was found within the frontal sinuses. Throughout the osseous system as a whole, and in the skull in particular, the small vascular foramina were opened out, and there was an increase in size of the venous sinuses.

In the occipital region of the skull were the following changes: The nuchal muscle area was increased in extent, and the external occipital protuberance, not only increased in size by bony deposit, but also moved upward a distance of from 8 to 10 mm. A most significant observation in this region was the relative displacement of the foramen magnum. Hypertrophy of the basilar part of the occipital bone displaced the foramen backward in giant acromegalics, while atrophy of this part, in non-giant acromegalics, moved the foramen forward. Also, in the late and atrophic stages of the disease, the head might be carried more extended on the neck, owing to change in shape of the occipital condyles.

There was great supra-orbital growth, with thickening of the bone and expansion of the frontal sinuses. The whole orbital region grew forward, owing to the great temporal development, which was due to or coincident with the great changes that took place in the mandible. Above, this forward orbital growth could be seen in the distance of the cribriform plate to the glabella, which, normally 14 mm., might become 25 mm.; and below, where the external angular process of the frontal bone and the ascending process of the malar bone might come to occupy a position 10 to 15 mm. farther forward and downward than normal. From these changes resulted the large prominent nose in acromegaly.

The zygomatic arch was increased in depth and lowered in its relationship to the cranial cavity. The normal inter-zygomatic diameter of 130 mm. might be increased to 154 mm.; and the external auditory meatus was also lowered. By such means the temporal fossa was greatly increased in size, as was also the area of origin of its contained muscle—in an upward and backward direction on the parietal bone 10 to 25 mm. more than normally the case. But it was the forward extension of the temporal muscle origin that was the most striking, for he found that the temporal ridge might be carried forward till it lay on a plane anterior to the anterior pole of the brain, instead of being, as normally, 15 to 20 mm. posterior to that plane. He concluded that this was the cause of the forward growth of the orbital region.

The inter-orbital distance might be increased from 3 to 5 mm. and the outer or-

bital wall might move outward and downward from 8 to10 mm.

The upper face (nasion to maxillary alveolar margin) he found increased in length, and might be 90 mm. instead of the normal 70 mm. This, however, was made up in great part by alveolar growth.

The symphysis of the lower jaw was increased in depth and, summarizing the facial deformity, he said: "The total increase in face length is about 20 mm.; the increase from one angle of the jaw to the other rather less (than 20 mm.)."

Keith found that the area of the palate is not increased in acromegaly, and may be even diminished, especially the palatal area of the lower dental arcade. In the lower jaw the width between the last molars was increased, in the mean 10 mm. The lower canine teeth were advanced till they were nearly in line with the upper incisors. An increase in porous vascular bone on the alveolar margins separates the teeth, and adds to palatal height.

In the mandible, the changes in the body of the bone were growth of the alveolar margin; growth at the mental eminence, and growth of the body of the bone, anterior to the groove for the facial artery. The chief changes, however, took place in the ramus. It became narrower and longer. Resorption occurred at the angle, producing the well-known "opening out" and bone was resorbed from the inner and deposited on the outer aspect of the angle, so that the rami seemed to move apart. The mandibular rami became lengthened by growth which took place at the condyle, coronoid process, and sigmoid notch. The floor of the glenoid cavity was thickened and the articular eminence diminished.

The foregoing summary of the various features of cranial pathological anatomy in acromegaly, to which pathologists and anatomists had called attention in the past, forms a sound guidance for the radiologist. However, we thought it essential, if we were to be certain of the truth of subsequent radiographic interpretation of minor degrees of change, that a preliminary study be done on documented, museum acromegalic crania, so that comparison could be made between the structure and dimensions of the dried skulls in reality and the data obtainable from the skiagrams of those skulls. It was also most desirable to study as many varieties and combinations of the pathologic changes as possible, and there were technical advantages in first examining dried crania, in that finer bone detail could be got than in cases of living subjects with the disease.

In addition, there was the decided advantage of making available, as standards for the radiologist, skiagrams of crania the study of which, both by the anatomist and the pathologist, had formed the foundations of our knowledge of the pathologic processes in this disease, as they affect the skull.

We were aware, of course, that such material would be by no means abundant, even though Atkinson (23), in 1930, after a laborious search of the world literature, had been able to find 1,319 cases of acromegaly, in 265 of which postmortem reports had been made. But we were not prepared to find such material so scarce as it subsequently proved to be. Twelve of the leading American anatomical and pathological museums, where large collections of crania were known to exist, were communicated with, while widespread inquiries were made about such material in universities and medical schools.

Only four acromegalic crania could be found in the United States. Two specimens (No. 1784 and No. 61) are from the Warren Museum, Harvard Medical School. These are of two patients of Dr. Harvey Cushing and the postmortem findings have been fully described (24). One specimen (No. 1145.00) is in the Mutter Museum, Philadelphia, while the fourth is in the Museum of the Department of Anatomy, University of Chicago; this is the skull of Dr. Dean Lewis' case (25).

To the curators of these museums we are deeply indebted for the opportunity given us to radiograph and study these specimens.

To the Curator of the Museum of the Royal College of Surgeons of England we

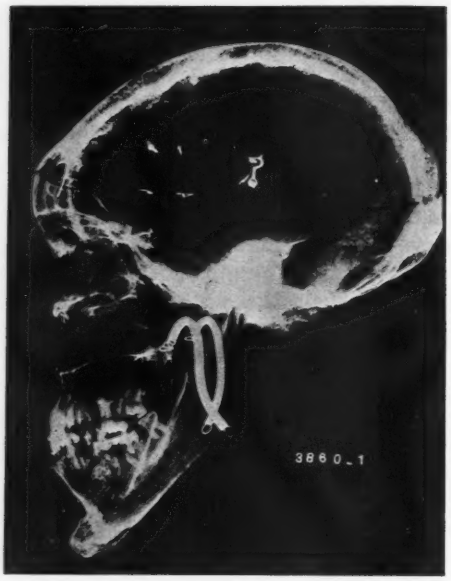


Fig. 2. No. 3,860–1, Royal College of Surgeons' Museum, London. Case presented by Dr. Frank Corner, 1912. Patient was male, aged 42 years, who died of acromegaly of over 17 years' duration.

are similarly indebted for the opportunity to study and radiograph six specimens, four of which were fully described by Sir Arthur Keith in 1911 (21).

To Professor J. C. Brash, Edinburgh University, we owe the opportunity to examine the cranium of the case reported by Cunningham (26), the skeleton of which was described by Thomson (18). The skiagram of this skull we owe to the courtesy of Dr. Duncan White.

Thus we have 11 documented specimens of acromegalic crania for roentgenologic examination. We shall describe them from the radiologist's standpoint, adding such clinical and descriptive data from other sources as will enable the reader to gain a more accurate idea of their condition.

For descriptive purposes we have found it convenient to arrange them in three major groups or types, according to the general picture of change observable in them.

Type 1.—This type is characterized by a generalized and marked degree of "expansion" of the medullary cancellous tissue of the bones of the cranium and face, with marked enlargement of those structures normally developed in the cancellous tissue of certain bones—the paranasal and mastoid air cells. In this type the resorption of bone has been very active, but deposition has at least succeeded in preserving the architectural structure, especially in the calvaria, so that the three tables of bone can clearly be made out, with a marked relative, as well as absolute, increase in diploe, and at least some rarefaction.

Figure 2 is the lateral skiagram of specimen No. 3,860–1, presented to the Museum of the Royal College of Surgeons, London, in 1912, by Dr. Frank Corner. The following facts are from the Museum Catalogue: The patient, who died of acromegaly at the age of 42, showed well marked signs of the disease at the age of 25 years, and was bedridden during the last ten and a half years of his life. Most of the bones of the limbs show signs of osteo-arthritis. His height, measured after death, was 1,843 mm. (6 ft. 0.5 in.).

"The facial portion of the skull is relatively large as compared with the cranial portion, the main increase being in a vertical direction. The superciliary region projects prominently forward, the distance from the middle of the external auditory meatus to the glabella being increased (145 mm.), and also the length of the cranium 203 mm. The superciliary projection produces the effect of a receding forehead, but otherwise the cranium is fairly normal in size and form (circumference, 568 mm.; breadth, 147 mm.; height, 130 mm.). The temporal lines are situated high up on the parietal bones, those of the opposite sides approaching to within an inch, immediately behind the bregma. The tympanic plate is thick. The mastoid process is large and its muscular attachments well marked. The occipital condyles are flattened and surrounded by ridges of new bone, resulting from osteo-arthritis. The frontal sinuses are expanded, and the two tables of bone forming the roofs of the orbits are widely separated in the greater part of their extent. The central part of the middle fossa is greatly deformed by the pituitary tumor. The pituitary fossa cannot be recognized; the body of the sphenoid bone is reduced to a narrow, median bony ridge and the sphenoid sinuses are almost completely obliterated.

"The orbits are large (height and width, 46 mm.) and the distance between their inner walls increased. The bi-zygomatic diameter of the face is 147 mm. (normal, 130 mm.). The superior maxilla is increased in size, especially in the vertical direction.

"The lower jaw is greatly elongated, measuring 168 mm. from the condyle to the point of the chin, and the lower alveolar border with its teeth projects beyond the upper, in the incisor region. The lower incisor teeth are widely separated. The increased size of the jaw is mainly due to enlargement of its body, both in length and thickness; the rami are relatively unaltered, except for considerable lateral enlargement of the condyles.

"The symphysis measures 48 mm. The angle formed by the ramus and the body is more open than normal. The length of the hard palate is 67 mm.; its width between the outer surfaces of the bone, at the level of the second molar teeth, is 70 mm. The tuberosities of the palate bone are hypertrophied."

The lateral skiagram of this skull (Fig. 2) gives a clear illustration of the foregoing description, and, in addition, it demonstrates the nature of the structural changes in the bones of the cranium and face. Clearly, this is a relative increase in cancellous bone, produced by an "expansion" of medullary spaces, resorption having been dominant while bony deposition was diminished, variable in amount, and irregular in situation.

In the vault this change manifests itself as "diploic expansion." The frontal bone is most affected, the parietal bone, as it is followed backward, decreasingly so, while the occipital bone, except for considerable thickening in the region of the lambda and external occipital protuberance, is least affected. The upward (backward) displacement of this last structure is clearly seen.

The frontal sinuses are very large and the degree of their extension into the orbital roofs is clearly evident. Their anteroposterior dimensions explain the superciliary bulging, already referred to, which almost angulates the frontal bone outline at the upper limit of the sinus, doing much to produce the appearance of a receding brow.

The sphenoidal sinuses have been obliterated—the tumor had invaded them during life, and operation had not been done—and there is well marked sclerosis of the floor of the middle fossa. The petrous portion of the temporal bone is abnormally dense, and the destruction of the sella turcica is evident. The mastoid cells are large and the mastoid process demineralized, for which reason it shows up poorly in reproductions of the skiagrams.

The maxillary antra are large and extend in the hypertrophic alveolar processes far below the level of the nasal floor.

The mandible shows a general demineralization, with large expanded medullary spaces in the body, and even more marked expansion in the mental process, which is abnormally prominent. This cranium while not prognathic, is slightly progeniac.

A subvariety of this type, which we call Type 1, A, occurs when expansion changes predominate in the brow and face, without such change markedly affecting the vault of the skull, the calvaria showing either a relatively normal structure or, more usually, actual thinning of the bone, with or without slight relative increase in diploe. There would seem to be a tendency for this to occur when the disease runs a rapid course in the young, or it may occur as an atrophic form, in the late stage of the disease.

Such a skull is No. 3,861-2 (Fig. 3) in the Museum of the Royal College of Surgeons, London, presented in 1931 by the London School of Clinical Medicine, and previously described in detail by Keith (21) as the "Greenwich Skull," from which paper and the Museum Catalogue the following is quoted:

"The skull of a male acromegalic between 50 and 60 years. The facial part of the skull is markedly increased vertically, the nasion to the upper alveolar margin is 82 mm. (normal 70 mm.), the bones concerned in the increase being the superior maxilla and the rami of the lower jaw. The angle of the lower jaw is well marked and in no way opened out or widened. The anterior nares are increased in size from above down, and the hard palate is high. The nasal bones are prominent, but there is no abnormal forward projection of the alveolar

Fig. 3 (*above*). No. 3,861–2, Royal College of Surgeons' Museum, London, presented by the London School of Clinical Medicine, 1931. Previously described by Sir Arthur Keith (1911) as the Greenwich Skull. Patient was adult male, acromegalic, aged between 50 and 60 years. Note the thinned calvaria with relatively slight increase in diploe and the increased density in the frontal part.

Fig. 4 (*below*). No. 3,864–1, Royal College of Surgeons' Museum, London, presented 1931, by the London School of Clinical Medicine. Skull of young male acromegalic. Note the thinned calvaria with relatively well marked diploe.

processes, either of the upper or lower jaw, or of the chin. The frontal sinuses are large and the glabella and superciliary ridges prominent. (The distance from cribriform plate to glabella is 25 mm.; the normal is 14 mm.)

"The cranium is not greatly altered in shape; the cranial bones are thin—(frontal bone, 6 mm.; parietal, 8 mm.) and the sagittal and lambdoid sutures are closed. There is a 20 mm. increase in the inter-zygomatic measurement, the cranial capacity is normal—1,500 c.c. The nuchal muscle area is increased by 2,200 sq. mm. The sella turcica is enlarged measuring 21 mm., anteroposteriorly, 33 mm. laterally, and 11 mm. deep."

As this specimen could not be dismounted for radiography the lower jaw could not be clearly shown.

The skiagram (Fig. 3) shows the marked hyperpneumatization of the brow and face and the backward extensions of the frontal sinuses along the whole length of the orbital roofs, with the well marked sellar expansion. The thinness of the skull is very evident, but the diploe can be distinctly seen, especially in the frontal bone which is somewhat thicker and denser than the rest of the vault.

Another "Type 1, A," skull is No. 3,864–1, from the Museum of the Royal College of Surgeons, London, presented by the London School of Clinical Medicine (Fig. 4). The Catalogue states:

". . . a young Jew, the subject of acromegaly . . . the shape of the cranium is altered, being increased in width, more especially in the parietal region, and flattened from above down through elevation of the base (of the skull). The osseous tissue of the calvaria is thin, the diploe being almost entirely absent. A thin deposit of new bone covers the inner surface in the middle line and over the adjacent surfaces of the parietal bones. The sutures are ankylosed. The pituitary fossa is enlarged an inch, anteroposteriorly, and one and a half inches between the anterior clinoid processes. The internal base is flattened and increased in width, in the region of the middle and posterior fossæ. Small bony deposits are present in the middle fossæ. There is bony ankylosis of the cranium and atlas in almost its whole circumference.

"The facial part of the skull is elongated vertically, the nasal bones and the ascending processes of the superior maxillæ are prominent; the anterior nares increased in vertical measurement and the margin of the upper jaw markedly projecting. The condyles of the lower jaw are abnormally wide and, owing to

the increase in size of the whole bone, their distance from the symphysis is increased to six and a half inches. The alveolar border is much atrophied and everted. The angle (of the mandible) is only slightly marked, the ramus and body of the jaw being very slightly inclined to each other."

The skiagram (Fig. 4) shows the calvaria to be very thin and demineralized with, however, a certain amount of diploe, especially in the frontal bone. The frontal sinuses are large and extend about half way back in the orbital roofs. The nasal bones are long. The expansion of the sella turcica is marked and there is well marked density of the middle fossa of the skull, and of the petrous pyramids. The mastoid processes are long and finely porous in appearance throughout. The maxillary antra are surprisingly normal in size in view of the general deformity of the face, and the forward projection of the upper alveolar process is clear. The mandible shows a profound change and is extremely disproportionate to the maxillæ. The angle is very open, the mental process is very projecting, and the whole bone very demineralized.

Also in this category belongs specimen No.1145.00 in the Mutter Museum, Philadelphia, which we owe to the courtesy of Dr. Shenck. The skeleton is described as that of a "giant," and it is obviously from an acromegalic subject. The patient was 23 years old. His height is said to have been 2.30 meters, but this was considerably reduced by the lateral curvature of the spine. The femur is 65 cm., the tibia 55 cm., and the humerus 47.5 cm. long. The antero-posterior diameter of the chest is 43 cm., and none of the diaphyseal cartilages are ossified.

The cranium is very large, its capacity being given as 2,320 c.c. The skiagram (Fig. 5) shows that although the face is large, it is relatively proportionate to the very large brain-case. The calvaria is very thin and the diploe poorly seen, there being a moderately well marked sclerotic change, especially in the frontal bone. In view of the open epiphyses elsewhere it is interesting to note the bony synostosis of the coronal suture, which must be re-

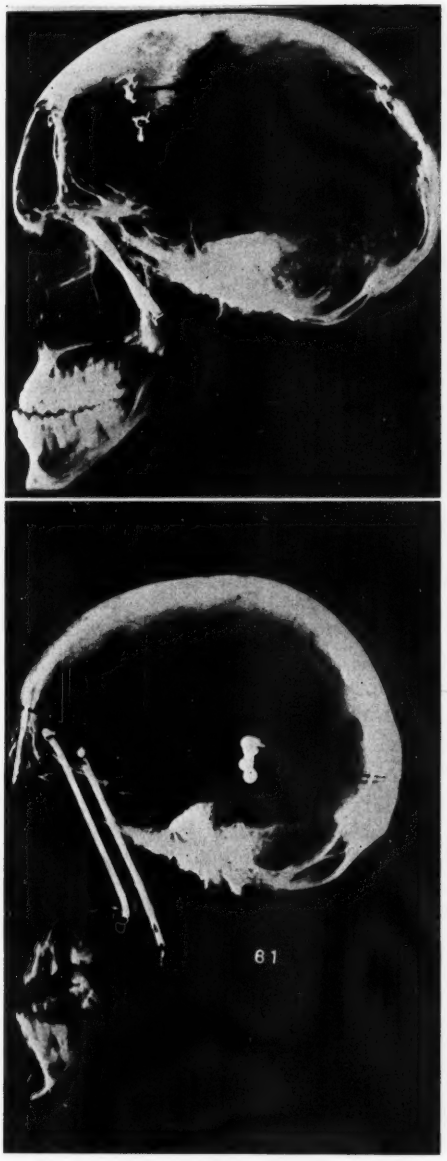


Fig. 5 (*above*). No. 1145.00, Mutter Museum, Philadelphia. Patient was acromegalic giant male, aged 23 years. Note the thinned calvaria and synostosis of coronal suture.

Fig. 6 (*below*). No. 61, Warren Museum, Harvard Medical School, presented by Dr. Harvey Cushing. Patient, G. B. S., male, aged 35 years. Acromegaly (chromophilic adenoma) 15 years. Note the calvaria is thinner in the frontal region.

garded as abnormal at the age of 23, and the somewhat spread lambdoid suture. The mastoid cells are both large and numerous; the petrous pyramid is dense, as is also the floor of the middle fossa.

The sella turcica is markedly expanded in the anteroposterior diameter, which may or may not have been due to an intrasellar tumor. From the appearance of the posterior clinoids, being somewhat drawn backward, the possibility does arise of an extra-sellar tumor producing this deformity by tension on the tentorium.

The frontal sinuses are enormous and extend far back in the orbital roofs; their walls are thin and very compact. They produce also a marked superciliary bulging, clearly evident over the root of the nose. The sphenoidal sinus is large and the maxillary antra abnormally so. The alveolar margin of the upper jaw is projecting; the mandible shows well marked progeniacism, the angle is moderately opened out, and more than a little demineralized.

In addition, the skeleton of this case showed well marked osteo-arthritic changes, especially at the hip joints.

We have also placed in this group (Type 1, A) specimen No. 61 in the Warren Museum, Harvard Medical School (Fig. 6.), one of the cases described by Cushing and Davidoff (24). The patient, G. B. S., a male, died at the age of 35 after 15 years of acromegaly. Pathologically, there was a chromophilic pituitary adenoma, with hypertrophy of the thymus, and adenomas in the thyroid, parathyroids, pancreas, and adrenals. The testicles were atrophic. He was 5 ft. 8 in. in height, and at one time had weighed 220 pounds. There was considerable adiposity and diabetes was uncontrollable.

The cranial skiagram shows that there is considerable elongation of the face but that the brain-case is by no means large. Anteriorly, the calvaria is thin, with a diminished diploic table, with considerable obliteration of the normal architectural structure by sclerotic change, which still more affects the parietal and posterior parts, where the calvaria is considerably thicker. For this reason the cranium might have been classed with the next type, but we have preferred to include it as a Type 1, A, because of the definite thinning of the frontal bone. This cranium weighed 485 gm., a point to which reference will later be made.

The frontal sinuses are large and extend well back into the orbital roofs. There is extensive damage to the sella turcica; the face is hyperpneumatized and elongated; the mandibular rami are very long, the angle is opened out, the mental process is expanded, and there is a marked demineralization of the face. The cranium is progeniac.

Another Type 1 specimen is No. 3,863-1, in the Museum of the Royal College of Surgeons, London, presented by C. F. Beadles in 1907, having been described by him in 1898 (22) and later by Keith, in 1911 (21).

"The patient, a huge bony woman, had died insane at the age of 40. She had large zygomatic processes, prominent superciliary ridges, and a receding forehead. The ears and lower jaw were immense, and she had spade-like hands and enormous feet. At autopsy it was noted that the body was very obese, the bony skeleton was huge, the thyroid was hypertrophied, and there was a cystic tumor of the pituitary, the size of a hen's egg, with great deformity of the sella.

"The calvaria is shallow and small and its bones unevenly thinned, in some places to the extent of being quite translucent. As one passes back, it tends to become thicker, and, at the posterior end, the specimen is a little over $\frac{1}{4}$ in. thick. In the thinned parts no diploe exists; in the thicker and hinder part the whole width seems composed of finely porous cancellous tissue. The coronal and sagittal sutures are distinct. Growing from the inner table of the frontal bone are a number of small dense bony outgrowths, of the nature of exostoses.

"The vault is very shallow, its highest point, only one inch behind the bregma, is scarcely two inches above the line of section (of the skull cap) . . . the frontal bone presents most peculiar changes. The forehead is very depressed and receding, there being no frontal eminences; it slopes gradually upward and backward to the coronal suture. The tem-

poral crest stands out prominently, giving a broad square contour to the forehead . . . it resembles the frontal region of the skull of an Australian aborigine, or that of one of the higher apes.

"There is an enormous distention of the frontal sinuses. For four inches across, the tables of the frontal bone are separated for a distance of an inch, both tables being exceedingly thin and translucent. The sinuses extend to within one and a half inches of the coronal suture. The weight of the dried skull cap is only 5 oz."

The skiagram (Fig. 7-*B*) in the postero-anterior view, shows the enormous extent of the frontal sinuses, the great prominence of the temporal crests, which form the lateral margins of the sinuses, and the general simian appearance of the skull cap. The lateral view (Fig. 7-*A*) shows synostosis of the coronal suture, the very thin sinus walls, and the very thin inner and outer tables, the greater part of the thickness in both the temporal and parietal portions of the vault being made up of very finely porous diploe. Keith gave the frontal and parietal calvarial thickness in this skull as 6 mm. in both regions.

To Type 1 also belongs the cranium of a skeleton in the Museum of the Department of Anatomy, University of Chicago. We owe this skiagram to the courtesy of Professor R. R. Bensley.

In 1931 this was a patient of Dr. Dean Lewis and a description of the skull was given by Bassoe (25) in 1922.

"He was a man of 40, 6 ft. 2 in. in height, and weighing 250 pounds. The circumference of the head was 635 mm., the binauricular arc 390 mm., and the distance from glabella to inion 400 mm. All sutures are obliterated. The superciliary ridges are markedly prominent . . . the external occipital protuberance, the mastoid processes and the superior nuchal lines also show marked bony overgrowth. The frontal, parietal, and occipital bones show hypertrophy which is greatest in their mesial portions, while the squamous portions of the temporal bones, and the greater wings of the sphenoid show no hypertrophy and are thinner than normal. The under surface of the base shows marked bony irregularities, at the seat of muscular and ligamentous attachments. The foramen magnum is encroached on by bony exostoses at the margin. A horizontal section of the skull shows thin external and internal tables with marked thickness of the diploe, both posteriorly and anteriorly and enormous dilatation of the frontal sinuses . . . which measure 5 cm. from above downward.

Figs. 7-*A* (*above*) and 7-*B* (*below*). No. 3,863–1, Museum of Royal College of Surgeons, London, presented by C. F. Beadles in 1907; described by him in 1898. Calvaria of insane female aged 40, the subject of acromegaly.

"A sagittal section of the vault shows a uniform thickness of 15 mm. with thick diploe and thin tables. The internal surface of the vault is markedly roughened, and shows a large number of flattened wart-like excrescences . . . especially abundant along the middle line . . . the sella turcica measures 36 mm. anteroposteriorly . . . the dorsum sellæ and posterior clinoids are destroyed, except for a small ridge at the base . . . the floor of the sella is destroyed and communicates with the sphenoidal sinus.

"The antra are greatly reduced in size. The alveolar processes and teeth are approximately normal. The malar bones and zygomatic processes are normal. The palate is markedly deepened, its roof very thin and narrowed in the transverse diameter . . . the inferior maxilla shows marked progeneum. There is marked elongation of the rami and the angle . . . is widened by 15 or 20 degrees. . . . There is moderate bony overgrowth of the margins of the symphysis of the chin, with a grooving of the anterior surface of the symphysis. The thickness of the body and the rami is considerably reduced, especially from groov-

Fig. 8. Cranium of acromegalic male from Museum of the Department of Anatomy, University of Chicago. Skiagram by courtesy of Professor R. R. Bensley.

ing along the mesial surface. . . . The condyles, necks, and coronoid processes are normal."

The lateral skiagram (Fig. 8) shows a "large" skull with a greatly elongated face. The frontal sinuses are huge, especially in their antero-posterior dimension, without extending to any great degree into the orbital roofs. They cause considerable supraciliary bulging. One half of the calvaria is missing, and in the remaining half the structure of the bone is clearly seen. Of the 15 mm. of bone which constitutes the calvarial thickness, about nine-tenths is seen to be composed of a finely porous diploe, the inner and outer tables being very thin. The thickest part is just above the frontal sinuses, and the calvaria diminishes slightly in thickness as it goes backward, the occipital part being the least affected. There is marked bony deposit on the external occipital protuberance. The mastoid processes are large and contain numerous large air cells, especially at the tip.

Damage in the middle fossa has largely obliterated the sella turcica and the sphenoid sinuses. The antra are not dilated. The palate is high, especially behind, and there is forward projection of the incisor portion of the maxillary alveolar process.

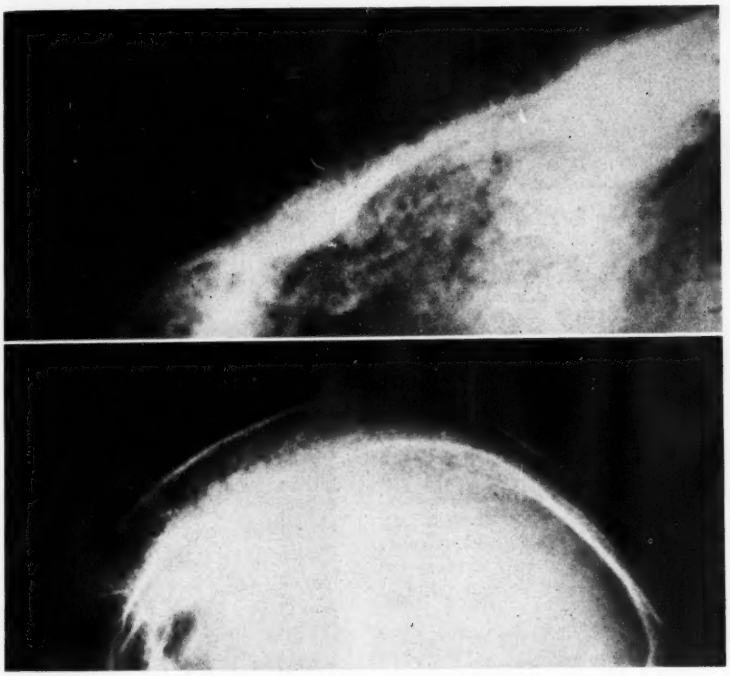
The skull is markedly progeniac, with elongation of the rami and body of the mandible, which have undergone cancellous expansion and atrophy by resorption; the mental protuberance is markedly expanded and projects forward beyond the body of the symphysis. The angle of the jaw is much opened out. There is hyperplasia of the mandibular alveolar process, especially in front.

The changes in this cranium are very closely similar to those found in the cases of Rowe and Mortimer (27) and Scriver and Bryan (28), both of which are Type 1 (Fig. 9-*B*).

Type 2.—Of the second group of acromegalic crania there are three specimens. The characteristic feature of this type is that, apparently having undergone initial changes similar to Type 1, there has subsequently occurred an excessive deposit of bone. It will have been noted, in the description of Type 1 crania, that the tendency is toward demineralization of the expanded cancellous bone, and that such deposition as does occur tends to be irregular and to favor certain sites. On the whole such crania are relatively light in weight for their size, and sometimes they are absolutely so, for resorption is dominant; in Type 2 deposition is dominant and extremely heavy skulls may be produced.

The increased density or "sclerosis" thus produced, appears in the skiagram as an increase in thickness and density of the inner table of the skull, the earliest and most marked site being the inner table of the frontal bone. As it progresses, it gives the impression of obliteration of the already expanded diploe, by outward extension of the sclerosis. By inward extension, calcification of the attached border of the falx is early seen in stereoscopic skiagrams, and later diffuse extensive exostoses may be formed on the inner aspect of the frontal eminences.

Such apparent outward extension is clearly seen in Rowe and Mortimer's case (Fig. 9-*A*), a male patient of 26, whose period of overgrowth had been from eight to sixteen years, and who ten years later was "apparently in a state of downward functional transition."



Figs. 9-*A* (*above*) and 9-*B* (*below*). Type 1, dysplasia. Calvaria of Rowe and Mortimer's case and of Scriver and Bryan's case, respectively.

The extent to which exostoses on the inner table of the frontal bone may occur is shown in Figure 10. This is the skull cap of a characteristic Type 2 change.

Although the facial bones in such crania may be somewhat denser than in Type 1 crania, the sclerotic process seems to be limited to the brain-case, and to arise from bone laid down by the cranial endosteum. It may greatly thicken all the bones of the brain-case, and even diminish the cranial capacity. The increased calvarial density demands, in skiagraphy, x-rays of considerably higher penetration, and it is for this reason that some of the skiagrams we show give the impression of a greater demineralization of the face than is actually the case.

As in the first type, there is also an increase in cancellous bone throughout the skull, with hyperplasia of the mastoid and paranasal sinuses. This would appear to be the earlier change, coincident with active bone resorption; and it would appear that the later sclerotic change is associated with what may be called the "functional involution" of a once hyperactive anterior lobe. We have discussed the mechanism of production of the sclerosis, in the light of experimental work, in another publication (28*a*).

An excellent example of this second type is the skull of Cunningham's (26) case (Fig. 11). The following points were noted by Thomson (18).

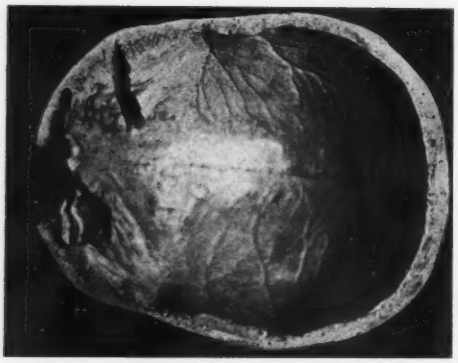


Fig. 10. Typical Type 2 calvaria weighing 500 gm. *Note:* The large frontal sinus on the right extends 20 mm. upward above the line of the saw cut, is 40 mm. laterally and 10 mm. in antero-posterior direction. The left sinus extends 12 mm. above the line of section, and is 25 mm. laterally. The right sinus extended far back in the orbital roof, the upper plate of which is attached to the specimen, and shows part of an ethmoidal bulla in the sinus.

"The subject was a male who died at 38 of diabetes. His height was 6 feet one-half inch. The bones of the skull were remarkably thick; the superciliary ridges were very pronounced and the frontal air sinuses of great extent. . . . . The pituitary fossa had undergone great expansion from the hypertrophy of the pituitary body" (Cunningham).

Thomson also noted

"the disproportionate increase in the dimensions of the face, which was more elongated than broadened, the chief increase being in the height of the superior and inferior maxillæ. There was prognathism, and, when viewed from above, the zygomata could be seen projecting on each side. The superciliary ridges, large and prominent, project beyond the glabella, and there was a deep depression at the fronto-nasal suture. The malar bones were prominent but there was no evidence of dilatation of the antra, described by Mr. Broca as characteristic of acromegaly, and as the cause of the prominence of the cheeks during life."

The skull was abnormal for Scottish skulls in length, breadth, and height, and the cubic capacity was considerably over normal, as was the external circumference. He labelled the skull "megacephalic" (1890). He gives the nasion-symphysis measurement as 148 mm., against a normal of 124.5 mm. derived from ten normal Scottish skulls.

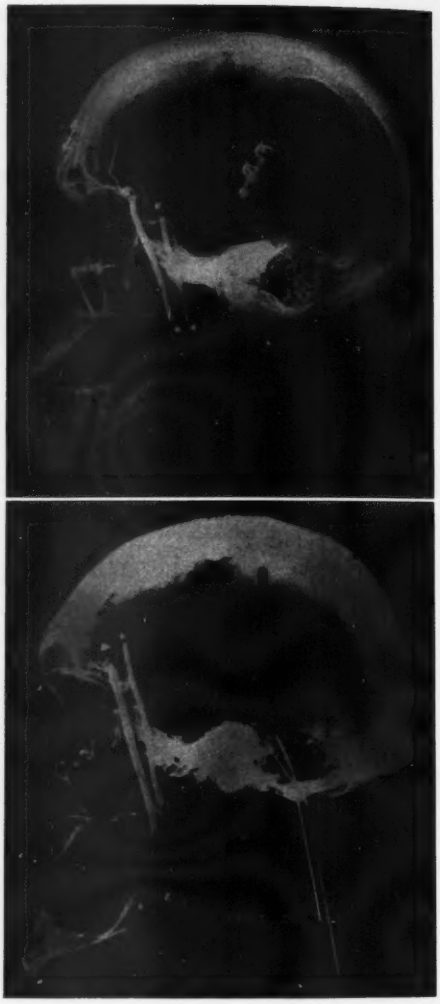


Fig. 11 (*above*). The Cunningham-Thomson Skull, from the Museum of the Department of Anatomy, Edinburgh University. Skiagram by the courtesy of Dr. Duncan White. Patient was male acromegalic, aged 36 years.

Fig. 12 (*below*). No. 3,861–1 in the Royal College of Surgeons' Museum, London. Described by Sir Arthur Keith as the Nicolucci Skull (1911). A modern Roman male skull the subject of acromegalic changes, age unknown.

There was extensive obliteration of the sagittal and lambdoidal sutures, all muscular ridges were prominent, particularly the median ridge of attachment of the ligamentum nuchæ, which was 6 mm. in height.

The orbits were enlarged, especially transversely. The upper jaw was vertically elongated, especially between the orbit and the alveolar border, and the latter margin massive and spongy. The palate was elongated, narrow, and deeply concave, and in the middle line showed recent new bone, perforated like a sieve by vascular foramina.

The mandible was very large and massive, the body very deep, and inclined forward at the symphysis. The rami were more increased vertically than anteroposteriorly, and the angle measured 112.5 degrees. The coronoid process was about a third higher than normal; the condyles were greatly increased transversely.

The cut surface of the calvaria revealed the thickness of the bones to vary from 6 to 12 mm. (note that this was not measured at the vertex) and both tables could be distinguished with intervening diploe, increased in thickness and density. Where the cut opened into the frontal sinuses, these were found dilated, the left measuring 45 mm. vertically and 35 mm. transversely, with the bone over them thick and massive, from bony deposition.

The sella turcica was enlarged, 22.5 mm. anteroposteriorly; 21 mm. transversely, and 18 mm. deep. The posterior clinoids were pushed backward and as thin as paper. The fossa was deepened at the expense of the sphenoid, which was only a quarter of its normal thickness vertically; its sinus was not enlarged.

The groove for the middle meningeal artery was deep and broad. Finally, he notes the diminution in size of the anterior fossa of the skull, by encroachment of the frontal sinuses and elevation of the orbital plates.

In concluding, he stressed the absence of dilatation of the mastoid, sphenoid, and maxillar sinuses in this specimen, in reference to Broca's pathological report on Marie's case, and sought to account for this difference by the sex and age of the patient. He failed, however, to note that, while his own specimen was sclerosed, Marie's case showed such marked decalcification that the os calcis "pitted with the finger"—it was a pure Type 1.

The skiagram of this specimen (Fig. 11) demonstrates clearly the calvarial thickening and increase of density, despite which the three tables can just be made out, with the great increase in relative thickness of the diploe, which is secondarily sclerosed. Although the frontal part is slightly more affected than the rest of the calvaria, the whole vault is much more uniform in thickness than is normally the case. There has been definite addition of bone at the external occipital protuberance. The frontal sinuses are large and extend into the orbital roofs, for about half their extent, but the detail here is somewhat confused by the presence of the wiring keeping the skull-cap in place. This latter provides a good objective standard of comparison of density for the structure of the calvaria.

The mastoid cells are large and numerous, a fact that can be made out despite the density of the overlying bone. The expansion of the sella turcica is clear, but the degree of development of the sphenoidal sinus cannot be made out, owing to the superimposed density of the sclerosed bone of the floor of the middle fossa. This sclerosis extends to the petrous pyramid.

The antra are not expanded, and the overgrowth of the alveolar bone of the upper jaw in front, with its inclination forward, is well seen. The face is not progeniac; the mandible does not overshoot the upper jaw.

The second skull in this group is No. 3,861–1, in the Museum of the Royal College of Surgeons, London, in which Type 2 changes are present in extreme form.

This skull is described by Keith (21) as the Nicolucci Skull, some of the significant measurements of which he gives: cribriform plate to glabella, 24 mm. (normal, 14 mm.); nasion to maxillary alveolar margin, 90 mm. (normal, 70 mm.); inter-zygomatic diameter, 154 mm. (normal, 130 mm.); calvarial thickness, in frontal region 15 mm., in parietal 15 mm. The

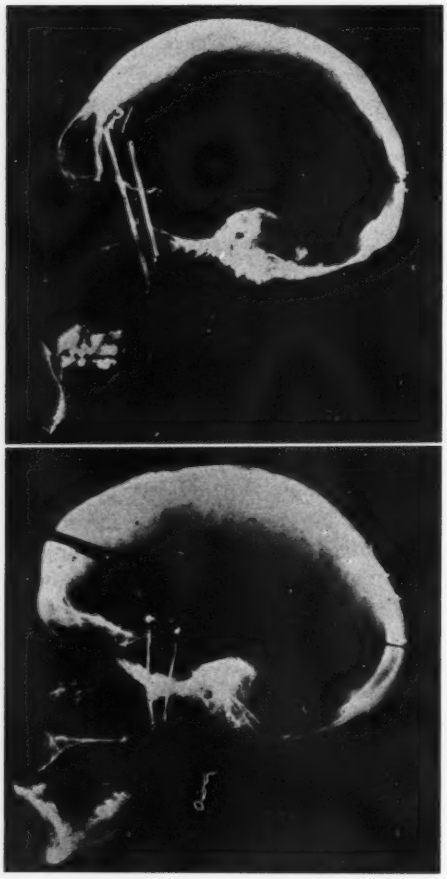


Fig. 13 (*above*). No. 1,784, in the Warren Museum, Harvard Medical School. Presented by Dr. Harvey Cushing. Skull of male acromegalic, aged 40 (chromophilic adenoma). Disease lasted 27 years. Note the great thickening and increased density in the frontal region of the calvaria. Skullcap weighed circa 500 grams, the whole skull (dried) 1,048 grams. Compare with Figure 6.

Fig. 14 (*below*). Nos. 3,862–1 and 3,862–2, in the Museum of the Royal College of Surgeons, London. Presented in 1911 by J. Thomson Walker and described by Keith (1911) as the Thomson-Walker Skull. Skull and calvaria of female, about 40 years of age, showing atypical acromegalic features.

Museum Catalogue gives the following facts:

"A modern Roman skull (male). The skull is unusually massive in consequence of a diffuse thickening involving the frontal, the parietal, and all the bones entering into the formation of the roof and sides of the cranial cavity. The thickened bones are dense and, for the most part, unnaturally porous, superficially, and slightly roughened, the surface changes being less marked over the area corresponding with the origin of the temporal muscles. Although the circumference of the skull is 570 mm., its capacity is but 1,500 c.c. The parietal bones, where thickest, *viz.*, in the neighborhood of the interparietal suture, measure 20 mm., and in section are closely cancellous, or compact without distinction of tables or diploe. The pituitary fossa is considerably enlarged, proving the existence of pituitary disease. The posterior part of the sagittal suture is obliterated.

"The lower jaw is markedly enlarged, but without such thickening as could be called massive. The length of the vertical ramus is increased, the chin pointed and unusually prominent. The general enlargement, however, is evident in the divergence of the posterior margins of the vertical rami, and in the increase in the lower dental arch, which everywhere exceeds the upper."

In the skiagram (Fig. 12), the enormously increased thickness and density of the calvaria are obvious, with complete loss of all architectural structure. The confining of this sclerotic change to the brain-case is striking. Along the vertex the superficial porous bone is seen as a somewhat striated or woolly outline, recalling somewhat the appearances in Paget's disease.

The mastoid cells are large and numerous, the sella turcica is markedly expanded, and the frontal sinuses are abnormally large, extending about half-way into the orbital roof. The sphenoidal sinuses cannot be made out clearly, but the maxillary antra, although well pneumatized, are not abnormally large.

The mandible is not heavy, although, like the whole face, it is considerably overpenetrated by an exposure which was intended to show up the architectural structure of the calvaria. There are two or three large medullary spaces in the prominent mental process. The angle of the jaw is opened out and there is progeniacism.

The third Type 2 skull (Fig. 13) is specimen No. 1,784 in the Warren Museum, Harvard Medical School, presented by Dr. Harvey Cushing (24). It is the skull of Mr. Van W., an acromegalic who died

at the age of 40, when his height was 6 ft. 6 in. and his weight 269 pounds. Vigorous growth began at 13 years and at 19 he was 6 ft. 4 in., weighing 200 pounds. At that age he was powerful, intelligent, and with uncontrolled libido. At 32 he was weak, drowsy and impotent, and had glucosuria. In the next three years he increased in weight and became practically blind. The glucose threshold was 300 gm. The tumor was a chromophilic adenoma.

Apart from the huge frontal sinuses, the increase in length of the face, the progeniacism and the local destruction in the middle fossa of the skull, the outstanding feature in this specimen is the great calvarial thickening, with marked increase in density, which most affects the frontal bone and results in such a degree of sclerosis that the skull cap alone weighs close on 500 gm., while the whole skull weighs 1,048 gm.

In this respect it is interesting to compare this skull with the other specimen from the same source shown in Figure 6 (Warren Museum, No. 61). Both were cases of chromophilic pituitary adenoma. The general facial deformity is very similar. In No. 61 the frontal sinuses are large, but not huge as in No. 1,784. It is, however, in the calvaria that the striking difference between the two crania is seen. In the former, the frontal bone is thin, the diploe being poorly developed and somewhat sclerosed, the skull cap weighing 215 gm. and the whole skull 485 gm., while in the latter the frontal bone diploe had undergone considerable early expansion, followed by such marked sclerosis that the skull cap weighs as much as the other skull complete.

It is clear, that, whatever the clinical and histological similarities in the two cases may have been, there must have existed, probably over a long period of time, a marked difference in the calcium metabolism, as shown by the calcium reserve in the bones—a difference, as far as the skull is concerned, most evident in the frontal component of the calvaria.

Type 3.—Of the eleven acromegalic crania there remains one which cannot be classified with either of the two foregoing types. It is specimen Nos. 3,862–1 and 3,862-2 (the calvaria) in the Museum of the Royal College of Surgeons, London. presented in 1911 by J. Thomson Walker and described by Keith (21) as the Thomson-Walker skull. The following details are from Keith's paper and the Museum Catalogue.

"The skull and calvaria of a woman, supposed to have been about forty years of age, who died in Vienna, the clinical history being unknown. The specimen shows marked enlargement of the pituitary fossa, with atypical acromegalic features. Anteroposteriorly the sella measures 19 mm., 22 mm. in width, and 14 mm. in depth. From cribriform plate to glabella is only 15 mm. (normal 14 mm.). From nasion to maxillary alveolar margin is 71 mm. (normal 70 mm.); the inter-zygomatic distance is 124 mm. (normal 130 mm.), and the cranial capacity is only 1,200 c.c. (normal 1,540 c.c. for adult male). The frontal and parietal bones are thickened and sclerosed, but there is an absence of any pronounced supra-orbital ridges, and the upper part of the forehead is not unduly shelving. The frontal sinuses are small. The palate is increased in area, and there is an increase in height in the alveolar process of the lower jaw, accompanied by some change at the angle, and increased height of the ramus. There is but little elongation of the face, or increase in mental prominence. The muscular depressions on the base of the skull are exaggerated. Where the frontal bone is thickest it measures 15 mm."

The lateral skiagram (Fig. 14) shows a small skull whose facial part is not large in proportion to the small brain-case; in fact, the upper part of the face, if anything, seems small in comparison. The frontal sinuses are hypoplastic, having reached only the size of those of a girl of about ten years. The damage to the sella is obvious; the antra are not expanded, and the maxillary alveolar process projects forward to a moderate degree. The mandible is moderately progeniac.

The striking feature in this case is the thickening and great increase in density of the calvaria. This most affects the frontal and parietal parts, the occipital part much

less. The brow has almost the vertical slope of childhood, a fact that is in accord with the almost infantile frontal sinuses, another fact that is very surprising in an acromegalic cranium. An impression of the great density of the bone, which seems to have occurred as an internal deposit and may account in part for the small cranial capacity, can be got by noting that it is almost equal to the density of the metal rods supporting the specimen.

At first we were rather nonplussed by the marked lack of certain of the outstanding features of the other acromegalic crania in this series, such as marked enlargement of frontal sinuses and increase in length of the face. Despite the evidence of damage to the sella turcica and the mandibular changes, the possibility arose, in the absence of a clinical history, of there being an element of Paget's disease present. Accordingly, we were very doubtful of the possible value of this specimen as a guide to the recognition of pituitary influence, in the lesser degrees of change in cranial form and structure. Contrary to our expectations, however, this specimen has proved to be of the greatest importance, although it was not until we had examined many hundred cranial skiagrams that we began to appreciate it.

In the light of 71 cases in our series, which showed changes similar in nature but less in degree, the great majority of which were women showing adiposity as well as other symptoms of pituitary failure in the later stages, we have little hesitation in concluding that such a cranium is produced by a dyspituitarism, in which the hyperfunctional phase is slight, transitory or non-existent and the hypofunctional phase is the long-lasting and dominant characteristic.

In this case we are inclined to think it probable that, in the second decade of life, the patient suffered from a pituitary hypofunction from which resulted the frontal sinus hypoplasia, and the onset of a calvarial sclerosis.

In cases in which small frontal sinuses are found in association with a thickened, dense calvaria, as in this case of the Thomson-Walker skull, we are inclined to think that this condition is due, not to the obliteration of sinuses that were once larger by the process of sclerosis, but to the fact that a condition of hypopituitarism was present during the years of active growth of the sinus, and that the part of the frontal bone, into which the sinus ordinarily would have extended, was similarly affected.

In the 500 dysplastic skulls in our series, we have seen no evidence of a frontal sinus, once formed, becoming secondarily obliterated, or even diminished in size, although the reverse process does occur, *i.e.*, a frontal sinus may become larger after the attainment of its full adult size, if a condition of active hyperpituitarism be present.

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(To be concluded)

PELLEGRINI-STIEDA'S DISEASE

A MANIFESTATION IN THE KNEE OF POST-TRAUMATIC CHANGES COMMON TO OTHER JOINTS[1]

By H. S. CALLEN, M.D., *Bradford, Pa.*

INTRODUCTION

PELLEGRINI-STIEDA'S disease is a post-traumatic disorder of the knee in which roentgen opacities appear near the internal condyle of the femur, but do not, as a rule, become manifest until two to three weeks after injury to the knee (1). Because each of the terms *calcification* and *ossification* have been applied to such roentgen opacities, confusion has arisen pertaining to which represents the true pathologic condition of this disorder. The exactitude of Pellegrini-Stieda's disease, as a disease entity, has also suffered because of conflicting reports pertaining to the structures of the knee it affects, and because similar changes occur about other joints after trauma.

Explanations will be proffered as to why para-articular calcification or ossification may occur after trauma, and a theory advanced pertaining to why certain joint structures seem more prone than others to become the seat of such pathologic processes. To indicate that Pellegrini-Stieda's disease is but a local manifestation of post-traumatic changes common to joints, attention will be called to points in common between it and other disorders in which para-articular deposits occur after trauma and form roentgen opacities about the involved joint.

PELLEGRINI-STIEDA'S DISEASE

Pellegrini, in 1905, first called attention to ossification of the tibial collateral ligament, and Köhler in the same year reported a similar case. Stieda, unaware of the previous work of Köhler and Pellegrini, drew attention in 1907 to a semi-lunar-shaped calcification seen about the superior border of the internal condyle of the femur (1). Thereafter numerous reports of so-called Pellegrini-Stieda's disease appeared in European medical literature, but no mention of the condition was made in our literature until July, 1932, when an editorial pertaining to it appeared in the then current issue of the "The American Journal of Roentgenology and Radium Therapy" (4). In 1933, Kulowski (5) was the first, in the English medical literature, to report a case of Pellegrini-Stieda's disease, since when 54 instances (4, 6, 9) of calcification or ossification near the internal condyle of the femur have been reported as having been observed in our United States.

Surely it has been the experience of others as well as myself to encounter additional cases of Pellegrini-Stieda's disease (Figs. 1, 2, 3), since our attention has been directed to the possibility of such a condition developing in the knee after trauma. Failure to have recognized this disorder more frequently is believed due to delayed roentgenographic appearance of the lesion (4).

Like other traumatic disorders, Pellegrini-Stieda's disease has a higher incidence in males (6), and resurrection, as it were, of this condition invites our serious attention to it and to analogous disorders because of possible medico-legal implications.

Pellegrini was under the impression that ossification followed trauma. Most observers are agreed that in this disorder ossification does follow trauma and that the injury may be direct or indirect in nature. Stieda attributed the condition to fracture with detachment of a small particle of bone at the moment of injury

[1] Read at the Twenty-second Annual Meeting of the Pennsylvania Radiological Society, Erie, Pa., May 21, 22, 1937.

with subsequent calcification taking place in the ligament (2). Others (9) are of the opinion that a fracture of the internal condyle of the femur might or might not be present and that ossification is due to metaplasia of connective tissue. König, Köhler, Pfister, and Ewald were definitely of the opinion that calcification seen in the ligament was a fractureless callous formation, and that it was the end-result of periosteal proliferation secondary to a tear in the ligament and tendons at that point as shown by the fact that the process never appeared within from two to three weeks after injury (3). Kulowski (5) believed that the clear space between the bony mass and the femoral margin demonstrated there was no need for periosteal participation in the formation of the mass.

The tibial collateral ligament seems to be most frequently affected (6), but different structures of the knee may be involved as was shown in Kulowski's patient in whom at operation the tibial collateral ligament was found to be free from pathologic changes which affected the adductor magnus and vastus medialis tendons (5). Andreesen (7) believed that calcification occurred in the attachment of the adductor magnus tendon. So opinions have differed concerning not only the site of involvement, but also the type of pathologic change produced in Pellegrini-Stieda's disease. These differences of opinion are not serious ones,

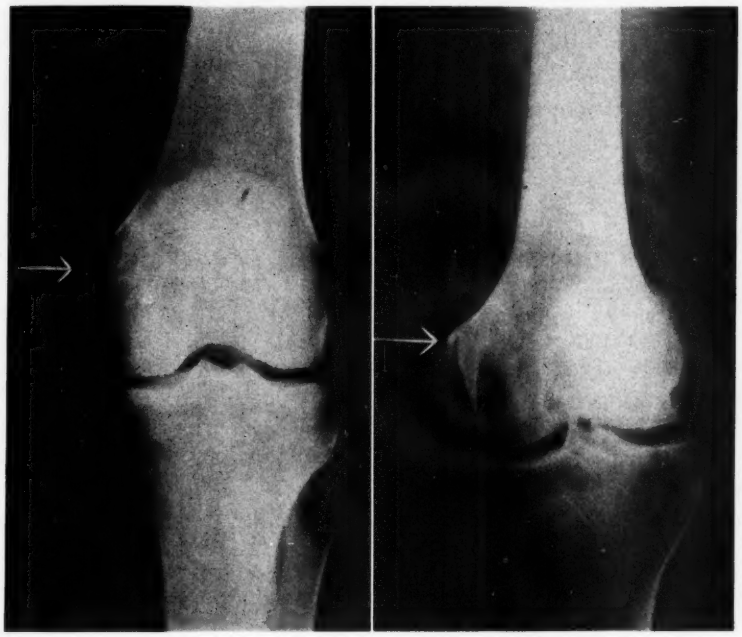

Fig. 1. Fig. 2.

Fig. 1. Early manifestation of Pellegrini-Stieda's disease, 20 days after injury, in a 50-year-old white male. A faint, semilunar-shaped shadow can be seen near the internal condyle of the left femur.

Fig. 2. Pellegrini-Stieda's disease in a 55-year-old white female in whom roentgenograms immediately after first injury to the left knee (July, 1933) showed no para-articular deposit. The above roentgenogram, made 20 days after second injury ($3^1/_2$ years after first), shows a deposit near the internal condyle of femur, the density of which suggests it to be the result of the initial and not of the recent injury.

Fig. 3 (*above*). Roentgenogram of right knee showing a proximal semilunar-shaped shadow and a smaller distal shadow near the internal condyle of right femur (14 months after injury), in a 49-year-old white male, in whom roentgenograms of the knee showed no evidence of this condition the day after injury.

Fig. 4 (*below*). Calcified subdeltoid bursitis in a 44-year-old white female. (No definite history of injury. Used simply as an illustration of calcified subdeltoid bursitis.)

being more or less of academic interest, but they nevertheless detract from the specific nature of the disorder as a disease entity, and since, as will be discussed later, other joints sometimes become likewise affected after trauma, the only feature to distinguish Pellegrini-Stieda's disease is its gross anatomic location, the knee.

SO-CALLED SUBDELTOID BURSITIS

Lewin (8) believed that calcification or ossification of the tibial collateral ligament was analogous to calcification of the supraspinatous tendon in the region of the subdeltoid bursa(Fig. 4). Until Codman (12), in 1906, clearly showed that the subacromial and the subdeltoid bursæ were identical and their names synonymous confusion existed pertaining to structural involvement in so-called bursitis of the shoulder. In this disorder there still is confusion pertaining to structural involvement, for some investigators feel that the initial lesion is always in the supraspinatous tendon, while others state that trauma is to the bursa at the time of abduction movements, the bursa being injured as it glides beneath the acromion (11). In this discussion we are concerned only with posttraumatic deposits, which in subacromial bursitis are not always due to calcification as shown by Case (13). He discovered such a deposit to consist of both bone and cartilage.

Analyses of calcium deposits in the body have revealed them to consist of calcium phosphate, from 80 to 85 per cent, and calcium carbonate from 15 to 20 per cent, the approximate percentages in which calcium salts occur in bone (10). Such equality of percentages explains the similarity in roentgenographic density of calcifications and ossifications of similar size, and points out the hopelessness of roentgenographic differentiation between the two, in the absence of trabeculation, justifying the use of either of these terms until such time when deposits as these can be identified histologically, if necessary.

Like the deposits occurring in so-called subdeltoid bursitis those developing in Pellegrini-Stieda's disease have been known

Fig. 5.

Fig. 6.

Fig. 5. Myositis ossificans. Bone laid down presumably in capsule of joint. No history of injury. (Illustration reproduced from "Diagnostic Roentgenology," Thomas Nelson & Sons, New York, 1936; Fig. 125, p. 361.)

Fig. 6. Para-articular ossifications in the knee of a tabetic. (Illustration reproduced from "Diagnostic Roentgenology," Thomas Nelson & Sons, New York, 1936; Fig. 139, p. 473.)

to disappear spontaneously or to disappear after the institution of physical therapy, while in other instances such deposits persist in spite of medical forms of treatment (1, 4, 6, 9, 11).

MYOSITIS OSSIFICANS

Kulowski (5) likened the bony mass found in his case of Pellegrini-Stieda's disease to that occurring in myositis ossificans. While myositis ossificans is not strictly a para-articular disorder, it occasionally occurs not far distant from joints, and sometimes after trauma. "Drill bone," common among enlisted men in the infantry, is a traumatic, circumscribed form of myositis ossificans occurring in the deltoid muscle of the shoulder. Myositis ossificans sometimes develops in the quadriceps femoris of football players after injury, and in the brachialis anticus after some posterior dislocations of the elbow, and is believed sometimes to affect joint capsules (Fig 5).

Myositis ossificans and Pellegrini-Stieda's disease have another point in common, in that recurrence of the pathologic process has been experienced after too early surgical intervention in either condition (5, 14).

PARA-ARTICULAR OSSIFICATIONS OF PARAPLEGIA

Ossifications have been found to occur about joints in some cases of paraplegia (Fig. 6) in which trauma has been held responsible. There are some who believe that tabetics *per se* develop bone in soft tissue at the slightest traumatic provocation, such as the prick of a hypodermic needle. Osseous deposits, however, occur about joints of paraplegics who are not syphilitics, and it has been assumed by some that in such instances rough handling by ambulance or hospital attendants has been responsible for the development of these deposits, just as use of joints in tabetics prior to the preparalytic stage of

their disease is thought to be the traumatic factor in such cases (10).

Paraplegia, then, regardless of its etiology, is another condition in which osseous deposits sometimes occur about joints after trauma.

SITES OF PREDILECTION

Particular ligaments or tendons of certain joints seem more prone than others to undergo calcification or ossification after injury. This is probably due, in part at least, to greater exposure of the ligament or tendon in question to direct or to indirect trauma.

PATHOLOGY

Some conditions have been stated in which calcific or osseous deposits develop about joints following trauma. Why calcification occurs in some and why ossification occurs in other instances, and why in still other cases neither of these pathologic changes develops after injury is at present inexplicable. Perhaps it will eventually be shown that trauma produces a local disturbance in tissue balance which, depending upon the prevailing state of glandular balance or the lack of it, results either in calcification or ossification in the latter, or in no pathologic change in the former instance. For the present it is pertinent that we pause for a moment to consider the manner in which calcification is believed by some to take place, and to review the different ways in which ossification occurs.

Calcification usually develops in tissues which are dead or in a state of reduced vitality as the result of some abnormal antecedant process, which as a rule is usually of an inflammatory nature. The conditions under which inflammation most frequently occurs are almost always associated with some form of injury. Fatty degeneration of cells frequently precedes calcification, and this might possibly account for the time interval elapsing between injury and the appearance of roentgen opacities. Calcium salts are obtained from the blood and lymph in which they are ordinarily held in solution. One theory propounds that when such solution

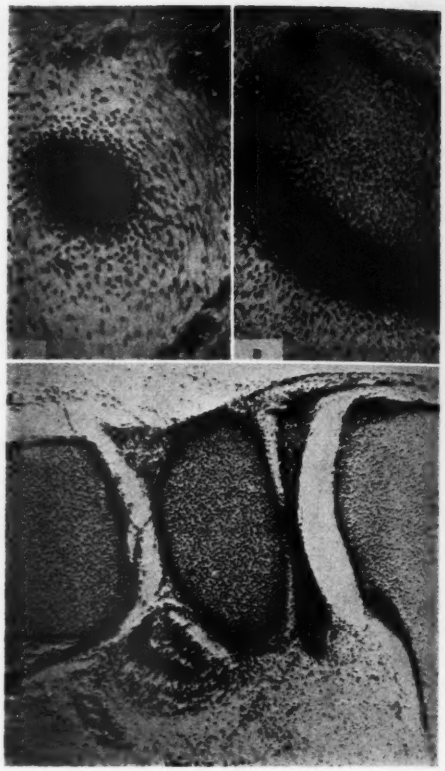

Fig. 7 (*above*). Photomicrograph of human embryo tissue × 140 mm. (*A*) shows the condensation of embryonic tissue (blastema) at the site of the future skeleton, and in (*B*) this precartilaginous condensation of connective tissue is giving rise at its center to early cartilage cells. The persisting rim of dense connective tissue about the early cartilage cells is the primitive perichondrium and has the power to form both bone and cartilage. Persisting strands identical in nature with the perichondrium are referred to as precartilaginous connective tissue. (Illustration and legend reproduced from "Tumors of Bone," C. F. Geschickter and M. M. Copeland, Revised Edition, Am. Jour. Cancer, 1936, Figs. 1-*A* and 1-*B*.

Fig. 8 (*below*). Photomicrograph of human embryo tissue × 140 mm. Low magnification of the bones about the knee joint. The bones have been preformed in cartilage. About this cartilage the dense embryonic connective tissue, which is the forerunner of cartilage, persists. Note that this early connective tissue is present in the future joint cavity and also adherent at the places where the tendons are forming. (Illustration and legend reproduced from "Tumors of Bone," C. F. Geschickter and M. M. Copeland, Revised Edition, Am. Jour. Cancer, 1936, Fig. 3.)

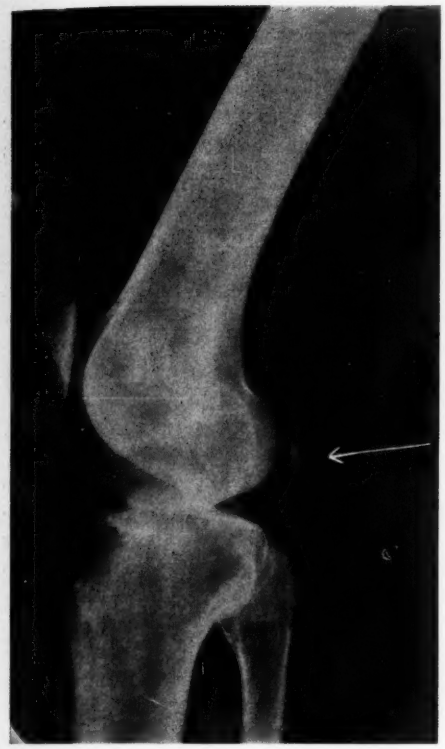

Fig. 9. Lateral roentgenogram of an adult white male showing a fabella in the left knee, presumably in the tendon of the gastrocnemius muscle.

comes into contact with fatty acids derived from the pathologic process of fatty degeneration, insoluble soaps are formed giving rise to calcific deposits in the tissue affected (15). Ligaments and tendons then, because, of greater exposure to direct or to indirect trauma are, therefore, probably more prone to become the depositories of insoluble soaps, as the result of injury.

Ossification—Bone is the most highly differentiated of the connective tissues. It is not a primary, but a secondary tissue being preceded either by cartilage or by fibrous connective tissue. That developed from hyaline cartilage is called endochondral bone, while that formed from fibrous connective tissue without the intervention of cartilage is known as intramembranous bone (16). Freund (5) found the following different types of bone to comprise the osseous mass in a case of Pellegrini-Stieda's disease; bone formed on the basis of connective tissue; bone formation which was callus-like in character, and endochondral bone.

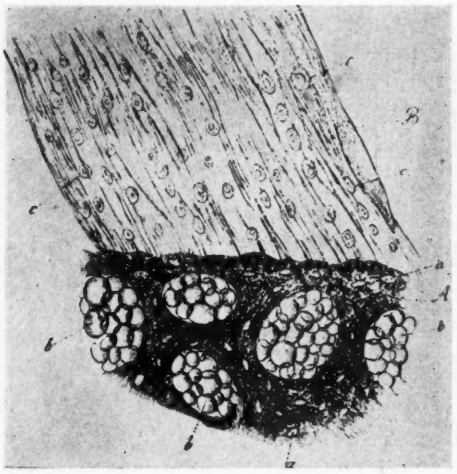

Fig. 10. This drawing depicts cartilage cells (*C*) in the end of the Achilles' tendon (*B*) which attaches directly to the bone of the os calcis (*A*). (Illustration after Kollicker, and reproduced from "Tumors of Bone," C. F. Geschickter and M. M. Copeland, Revised Edition, Am. Jour. Cancer, 1936, Fig. 23.)

Because fibrous connective tissue possesses power to form a special type of bone, and because fibrous connective tissue is the principal constituent of ligaments and tendons, these structures are inherently capable of producing intramembranous bone when so provoked, as by trauma, for instance; but to conceive how endochondral bone can form in ligaments or tendons necessitates a brief consideration of the histogenesis of joints.

Not only intra-articular tissues, but ligaments, tendons, and bursæ nearest the joint are derived from precartilaginous, or blastemal, tissue capable of forming both cartilage and bone. Mesenchyme destined to form both cartilage and bone condenses (Fig. 7) at the site of the future skeleton in the early embryo.

Strands of this tissue (Fig. 8) cut their way across the future bone at right-angles to it and persist at the site of future joints.

Fig. 11. Lateral view of left ankle of a 47-year-old male showing recent fracture of ossified tendo Achilles, ossification presumably having taken place after initial injury 15 years prior to recent injury which fractured the ossified tendon. (Illustration from "Radiography and Clinical Photography," D. M. Clark, December, 1936, **12**, 11.)

By mucoid regression some of this tissue forms joint cavity, the surrounding condensation of mesenchyme forming synovial membrane. Other strands persist at the reflection of the joint capsule and at its points of attachment to tendons and ligaments (14). So it is in this manner that ligaments, and tendons come to acquire inclusions of primitive tissue which evidently lie dormant in the sense of Cohnheim cell rests until stimulated, as by trauma, to undergo metaplasia. A sesamoid bone of the knee, the fabella (Fig. 9) is an example of endochondral bone arising from a primitive tissue inclusion in the gastrocnemius tendon. Kollicker (14), as early as 1853, depicted cartilage cells in the Achilles' tendon (Fig. 10), a location in which extra-skeletal ossification occasionally occurs (Fig. 11).

SUMMARY

1. Because confusion has arisen pertaining to which of the terms, *calcification* or *ossification*, represents the true pathologic condition occurring in Pellegrini-Stieda's disease, it has been pointed out that either calcific or osseous processes may develop about joints after trauma.

2. Attention has been called to the hopelessness of roentgenographic differentiation between calcific and osseous deposits of similar size in the absence of definite trabeculation, justifying the use of either of the terms *calcification* or *ossification* in reference to roentgen opaque deposits of such character.

3. Fatty degeneration, a pathologic process thought by some to precede calcification is suggested as a possible cause for the delay in the roentgenographic appearance of calcific deposits developing after injury.

4. The extra-skeletal formation of endochondral and of intramembranous bone has been briefly reviewed.

5. A theory has been advanced pertaining to why particular ligaments or tendons of certain joints seem more prone than ligaments or tendons of the same or of other joints, to become seats of ossification or calcification after trauma.

6. Analogies have been drawn between Pellegrini-Stieda's disease and some other disorders in which, after trauma, paraarticular calcification or ossification sometimes develops, indicating that the former condition is not truly a disease entity, but a local manifestation in the knee of posttraumatic changes common to other joints.

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HEREDITARY MULTIPLE ANKYLOSING ARTHROPATHY[1]

(CONGENITAL STIFFNESS OF THE FINGER JOINTS)

By A. R. BLOOM, M.D. *Detroit, Mich.*

From the Roentgen Department of the North End Clinic

HEREDITARY multiple ankylosing arthropathy is a rare hereditary condition in which there is ankylosis of the middle and proximal phalanges of the hands together with changes in other joints of the body, and it is due to a congenitally inherited abnormality of the cartilages between the joints. Genealogical investigation of the various cases reported in the literature proves that this anomaly is inherited according to Mendel's law. It is a distinctly dominant characteristic and not sex-bound. Drinkwater (1) has traced the genealogical tree of one family with stiff fingers through fourteen generations, and Révész (2) reported a case which he traced in three generations.

In 1932, Rochline and Simonson (3) described two cases of this rare anomaly in one family; they called it "congenital stiffness of the finger joints." They reviewed the literature which included reports by Rochline (4), Aschner (5), Duken (6), Drinkwater (1), and Köhler (7). Harvey Cushing (8) described this condition in 1916, in "Genetics" under the name of "hereditary ankylosis of the proximal phalangeal joints" (symphalangism).

The term "congenital stiffness of the finger joints" seems to me to be misapplied. It does not describe the condition accurately, for it is not limited to the finger joints; neither does "congenital stiffness" describe the cause nor convey the mechanism of the rigidity. I have suggested the term *hereditary multiple ankylosing arthropathy* as being more descriptive and informative.

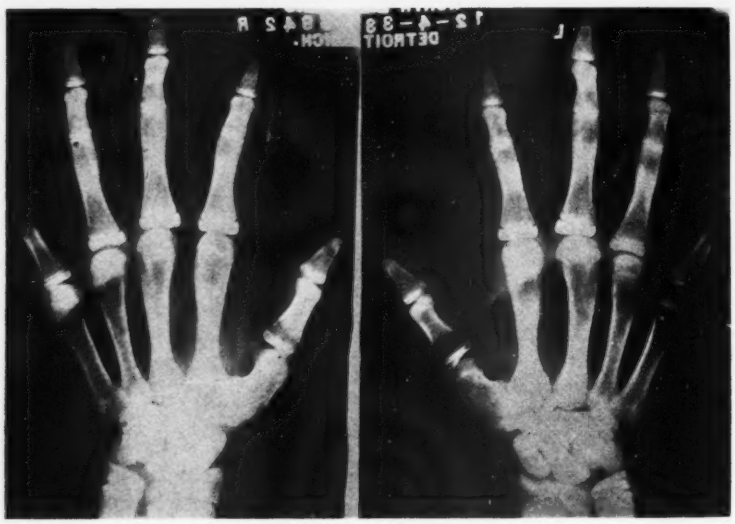

Fig. 1.

The joint involvement is readily apparent at birth and such joints as are free of abnormality at that time never ankylose.

[1] Read by title at the Twenty-second Annual Meeting of the Radiological Society of North America, at Cincinnati, Nov. 30–Dec. 4, 1936.

Fig. 2.

However, there is never any ankylosis at birth or in intra-uterine life. The roentgenograms of the newborn show the middle phalanges to be in very close approximation to the proximal phalanges. Anatomic and histologic examinations reveal a hypoplasia and sometimes an anaplasia of the joint structure. Usually it is symmetrical joints which are involved.

Cunningham describes the formation of the normal joint as follows:

"The primitive immovable joint is first recognized as a mass of undifferentiated mesodermic cells situated between the two masses,

Fig. 2-*A*.

which have differentiated into primitive cartilage.

"The cell mass which constitutes the joint-unit presents the appearance of a thick cellular disc, the proximal and distal surfaces of which are in accurate apposition with the primitive cartilages, while its circumference is defined from the surrounding mesoderm by a somewhat closer aggregation of the cells of which the disc is composed. From this cellular disc or joint-unit all the structures characteristic of amphiarthrodial and diarthrodial joints are ultimately developed.

"Within the substance of the disc itself a transverse cleft, more or less well-defined and complete, makes its appearance. In this manner the disc is divided into proximal and distal segments, separated from each other by an interval which is the primitive articular cavity. This cleft, however, never extends so far as to interrupt the continuity of the circumferential part of the disc which develops into the fibrous tissue of the investing ligaments. From the proximal and distal segments of the articular disc the various structures, distinctive of movable joints are developed."

Duken (6) who made the pathologic and anatomic investigation of this condition, came to the conclusion that the stiffness is due to the hypoplasia and sometimes anaplasia of the interphalangeal joint and these anomalies are produced as a result of insufficient and irregular differentiation of the intermediary zone of the pre-cartilage tissue. These changes in the joints result in varying degrees of bony ankylosis.

Ankylosis starts in childhood and early youth, becoming more marked as the subject grows older. At any one time various stages of ankylosis can be seen in various joints. (See Fig. 1.) Observers have been able to follow up all the stages to complete and solid bony union. Sometimes in

Fig. 3.

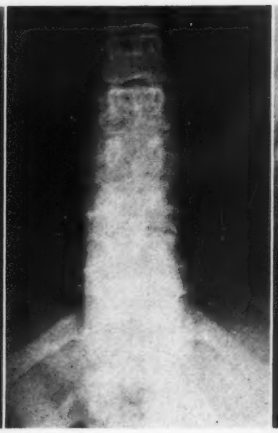

Fig. 4.

Fig. 5.

older individuals the ankylosis has been so complete that no sign of the early division could be recognized (see Fig. 2). At this stage there is a common bone marrow.

Although the condition is frequently termed "congenital stiffness of the finger joints," the fingers are never alone involved. All the cases reported have other joint abnormalities, but no case is without finger joint involvement. Four cases reported by Rochline and Simonson (3) were as follows:

The first case had, in addition to changes in the finger joints, similar deformities of the head of the second to the fifth metatarsal, bilateral subluxation of the head of the radius, bilateral coxa vara, flattening and increased transverse diameter of the twelfth dorsal, and all the lumbar vertebræ.

The second case had, in addition to the changes of the proximal phalanges, subluxation of the elbow joints and abnormalities of the metatarsals.

In another case there were changes of the facial bones, deformities of the thumbs and big toes, and ankylosis of all the phalanges of the feet.

In the case of an 18-year-old girl, the ankylosis of the finger joints was accompanied by changes in the soft tissue of the fingers, giving a ring-like form of indentations.

Our case had, in addition to changes of the proximal phalanges, complete ankylosis of the tarsal bone of the foot (Fig. 2), anterior subluxation and abnormalities of the heads of the radii (Fig. 3), flattening and broadening of the sixth dorsal vertebra (Fig. 4), wedging of the fifth, sixth, and seventh dorsal vertebræ, persistance of late epiphyseal plates, notching of the vertebræ (Fig. 5), and abnormalities of the carpal bones (Fig. 1).

The complete fusion of the tarsal bones of the foot has been reported before.

CASE REPORT

B. L., born in 1920, originally came to the North End Clinic in 1927 for ring worm infection of the scalp. In 1931 he was seen in the Pediatric Department because of enuresis. At that time he measured $59^1/_4$ inches and weighed $129^1/_4$ pounds. Because of his size and weight he was diagnosed as the pituitary type of endocrine disturbance, but x-ray examination of the skull revealed a normal sella turcica.

In 1933, he was referred to the Orthopedic Department because of painful feet of several years' duration. Examination by Dr. F. Fischer revealed very relaxed

Fig. 6 (two views).

pronated feet with prominent scaphoids. The feet were very rigid, and there was considerable peroneal spasm. There was tenderness along the longitudinal arches. The patient was referred to the Roentgen Department for radiographic examination of the feet, with a tentative diagnosis of spastic flat feet or calcaneonavicular colation. After the report given below was made, the boy was given a more extensive examination. It was found that the digits of the hand tended to spread. The little finger was deformed at the distal joint and adducted. There was a disturbance in the joint line as though the radial side of the epiphysis did not keep up with the ulnar. Similar, though less marked, changes were noted in the fourth finger. (All changes were symmetrical.) There was a bulbous enlargement at the distal phalanx of the index finger. Apparently there was an absence of interphalangeal joints of the fourth finger of each hand (Fig. 6). The patient was unable to close his fist. The elbow (Fig. 8) showed an increase of the carrying angle, with limitation of supination. Further examination of the feet showed the heels to be inverted. The feet were broad, flat and rigid, with about ten degrees inversion. The toe joint was present (Fig. 7).

On questioning the mother, we learned that several of the boy's maternal relatives had similar deformities.

ROENGTEN FINDINGS

Anteroposterior and lateral views of both feet (Fig. 2) show symmetrical changes. The arches are flat. Practically all the tarsal bones are fused into one solid mass, and very little, if any, demarcation of the individual bones can be seen. There is a separate bone between the base of the first metatarsal and the solidified tarsus, which I believe to be the cuneiform. The anterior aspect of the solid tarsus is straight and the posterior aspect of the cuneiform is in line with the bases of the second, third, and fourth metatarsals. The epiphyseal heads of the second, third, fourth, and fifth metatarsals are not united, and there are epiphyses present at the bases of the second, third, fourth, and fifth proximal phalanges. The third, fourth, and fifth toes have only two phalanges each. The second toes have three phalanges, the distal and middle being very small. There is an ununited epiphyseal plate at the base of the first distal phalanx. No epiphyseal plates can be seen between the distal and proximal phalanges of the other toes. The first metatarsal is shorter than the other metatarsals, although considerably broader. The combined length

Fig. 7.

Fig. 8.

of the first metatarsal and cuneiform is equal to the length of the other metatarsals.

Anteroposterior views of both hands (Fig. 1) also shows symmetrical changes. There is a marked abnormality of the first metacarpal. It is broad and irregular in shape. The base of the second metacarpal is broad and notched. The neck of the first metacarpal is rather broad and tapers to the middle, resulting in a spindle-shaped appearance. The joint space between the metacarpals and the proximal phalanges appears normal. The epiphyseal heads have not united nor have the epiphyseal plates at the base of the proximal phalanges. The joint spaces between the proximal and middle phalanges of the second, third, and fourth fingers are very narrow and atrophic and in the fifth finger the two phalanges are united. One cannot see the point of union. There appears to be a united central cavity. The joint space between the proximal and middle phalanges of the first finger of the left hand shows beginning ankylosis, but the joint space can be made out. The joint space between the middle and proximal phalanges is straight across and very narrow, presenting the appearance of a fixed rather than a movable joint. There appear to be six carpal bones present. There is one large bone which occupies the space of the capitate, lesser multiangular, and greater multiangular. This bone is triangular in shape and the base articulates with the first, second, third, and part of the fourth metacarpal. The hamate articulates with the fifth and part of the fourth metacarpal. The navicular is of normal size, but the lunate is rather small. The triquetrum is present but the pisiform cannot be made out. One bone about the size and shape of the pisiform lies below the bases of the fourth and fifth metacarpals. The distal epiphyses of the radius and the ulna are not united.

Anteroposterior and lateral views of the elbow (Fig. 3) show marked broadening of the condylar end of the humerus. The medial condyle is markedly enlarged and projects medially. There is evidence of an ununited epiphysis. The condyle on the radial side, by contrast, appears not completely developed; the head of the radius, instead of being flattened, is bulbular. The proximal epiphysis is not completely united. In the lateral view the trochlea of the humerus fits into the olecranon

fossa, but the head of the radius appears to be anterior to the humerus and interferes with complete flexion.

Anteroposterior views of the dorsal spine (Fig. 4) show the sixth dorsal vertebra to be rather flattened at the base. From the seventh dorsal to the base of the tenth dorsal vertebra, there is a fairly dense line about one eighth of an inch from either lateral aspect of the spine and parallel to the course of the spine. The ribs and the shoulder joint appear normal. Lateral view of the dorsal spine (Fig. 5) shows a wedging of the fifth, sixth, and seventh dorsal vertebræ. There is marked notching of the anterior aspect of these vertebræ and the epiphyseal plates are quite prominent and separate.

CONCLUSION

(1) Another case of a rare hereditary condition is reported.

(2) To the writer's knowledge, this is the first case reported in which there is complete fusion of the tarsal bones.

(3) The term *hereditary multiple ankylosing arthropathy* is suggested in the place of *congenital stiffiness of the finger joints.*

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CORRELATION OF SURGICAL AND ROENTGENOGRAPHIC FINDINGS FOLLOWING THORACOPLASTY FOR CHRONIC PULMONARY TUBERCULOSIS

By LEW A. HOCHBERG, M.D., C.M., *and* LOUIS NATHANSON, M.D., M.Sc., *Brooklyn, N. Y.*

From the Surgical Service of Dr. Pol N. Coryllos and Roentgenological Service of Dr. Henry K. Taylor, Sea View Hospital

THORACOPLASTY has become a routine surgical procedure for the treatment of chronic pulmonary tuberculosis, in cases in which other less radical measures have failed to yield the desired results. The medical profession at large and particularly roentgenologists, thoracic surgeons, and phthisiologists are being called upon daily to interpret roentgenograms of patients in whom this has been performed. To properly interpret studies of this nature, the surgical procedure must be understood and the sequelæ resulting therefrom recognized.

In recent years, few papers have appeared dealing with the roentgenographic findings following thoracoplasty, and these describe individual phases rather than the subject as a whole. The vast material at Sea View Hospital permits a detailed study of this subject from both the surgical and roentgenological standpoints. In this communication we will attempt to correlate the surgical procedure and the roentgenographic changes seen following thoracoplasty in the examination of post-thoracoplasty roentgenograms.

FIRST STAGE

The surgical procedure in this stage consists of the subperiosteal resection of the upper three or four ribs, beginning as close to the vertebral margins as possible. The osseous portions of the first and second ribs are generally removed *en toto*, and only small anterior portions of the third and fourth ribs are left behind. Occasionally, portions of the transverse processes are removed with the costal structures.

Roentgenographic examination following the first stage reveals anterior portions of the third and sometimes fourth ribs with the complete absence of the first and second ribs (Figs. 2, 6, 8, 12). The anterior remnants of the third and fourth ribs appear drawn backward, and the entire upper thorax in the area of rib resection appears narrowed. At times, the transverse processes appear irregular and sectioned, characteristic of surgical removal. The underlying lung is retracted downward and inward and appears airless (atelectatic) with its apex usually at the level of the third or fourth interspace (Fig. 6). Cavitation when visualized appears compressed and conforms to the general collapse of the lung (Figs. 5, 6, 11, 13). The mediastinum may be displaced slightly to the contralateral side, but not appreciably, and similarly the diaphragm may be somewhat depressed. The trachea as a rule is shifted considerably to the opposite side, but does not undergo any change in the caliber of its lumen. There is a scoliosis of the upper dorsal vertebræ with a convexity toward the side operated upon (Figs. 7, 8). Occasionally there is an anterior rotation of the lower cervical and upper dorsal vertebræ (Fig. 7). This rotation is away from the side operated upon. The scapula and clavicle at this time appear prominent with no appreciable change in position (Fig. 1). The immediate postoperative roentgenograms usually show considerable air scattered throughout the soft tissues of the area operated upon, extending into the neck and down the chest wall (Figs. 1, 4, 12). About the operative site there frequently is a collection of air and fluid which may assume various configurations. This is more commonly seen above and lateral to the collapsed lung (Figs. 1, 2, 8). Surgical dressings appear prominently on the roentgenogram and frequently a drain and skin clips may be seen *in situ* (Figs. 1, 2, 4, 12).

At the time of the surgical intervention, relatively large segments of rib are re-

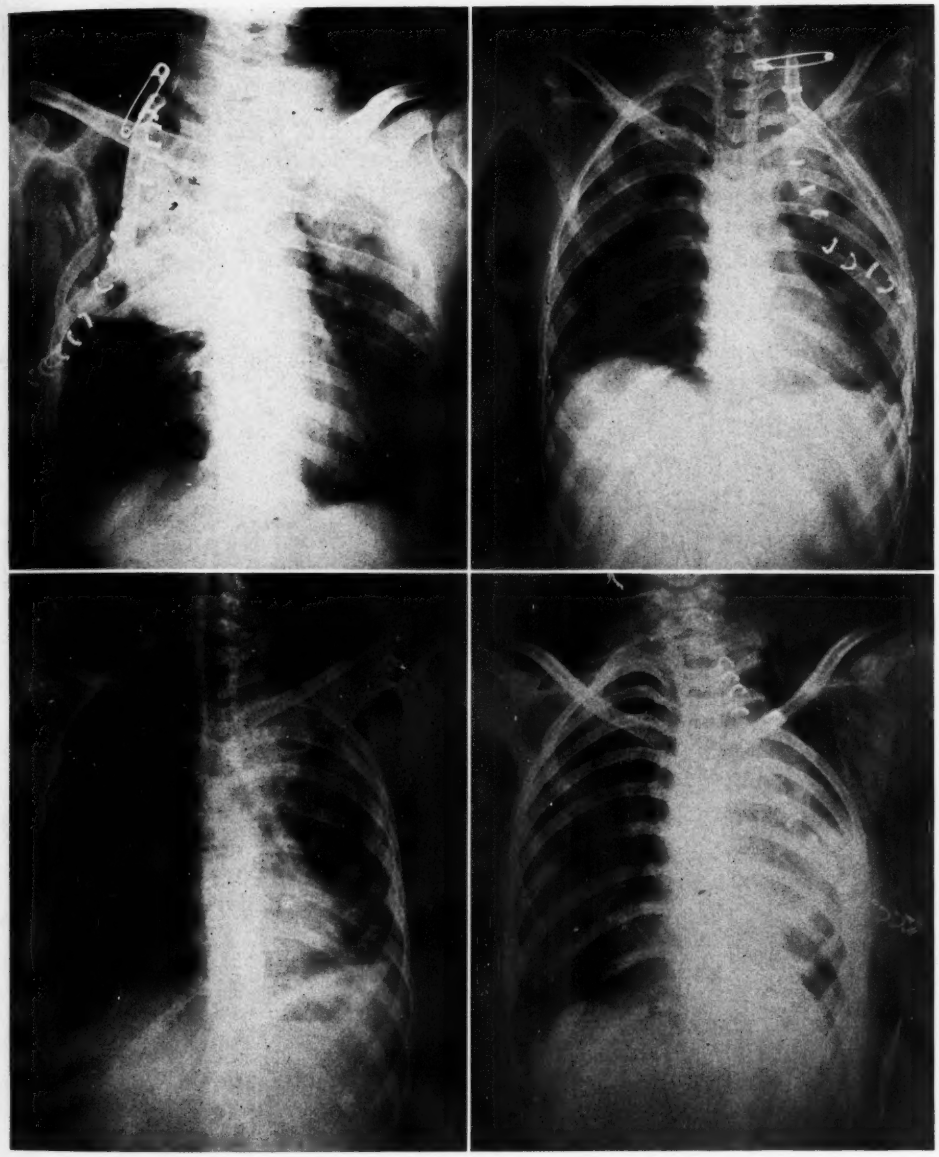

Fig. 1 (*upper left*).[1]
Fig. 3 (*lower left*). Same case as Fig. 2.

Fig. 2 (*upper right*). Same case as Fig. 3.
Fig. 4 (*lower right*).

[1] It is suggested that the reproductions in this article be viewed through a reading glass in order to visualize detail structures, etc.

moved so as to free the underlying soft tissues from the non-yielding bony thorax, thereby permitting the greatest anatomical collapse of the lung. The underlying lung, following this procedure, collapses down to the level of the third or fourth rib. Occasionally, the lung is adherent mesially, preventing this drop and thereby causing an inadequate collapse of the lung. In such instances, and in cases in which

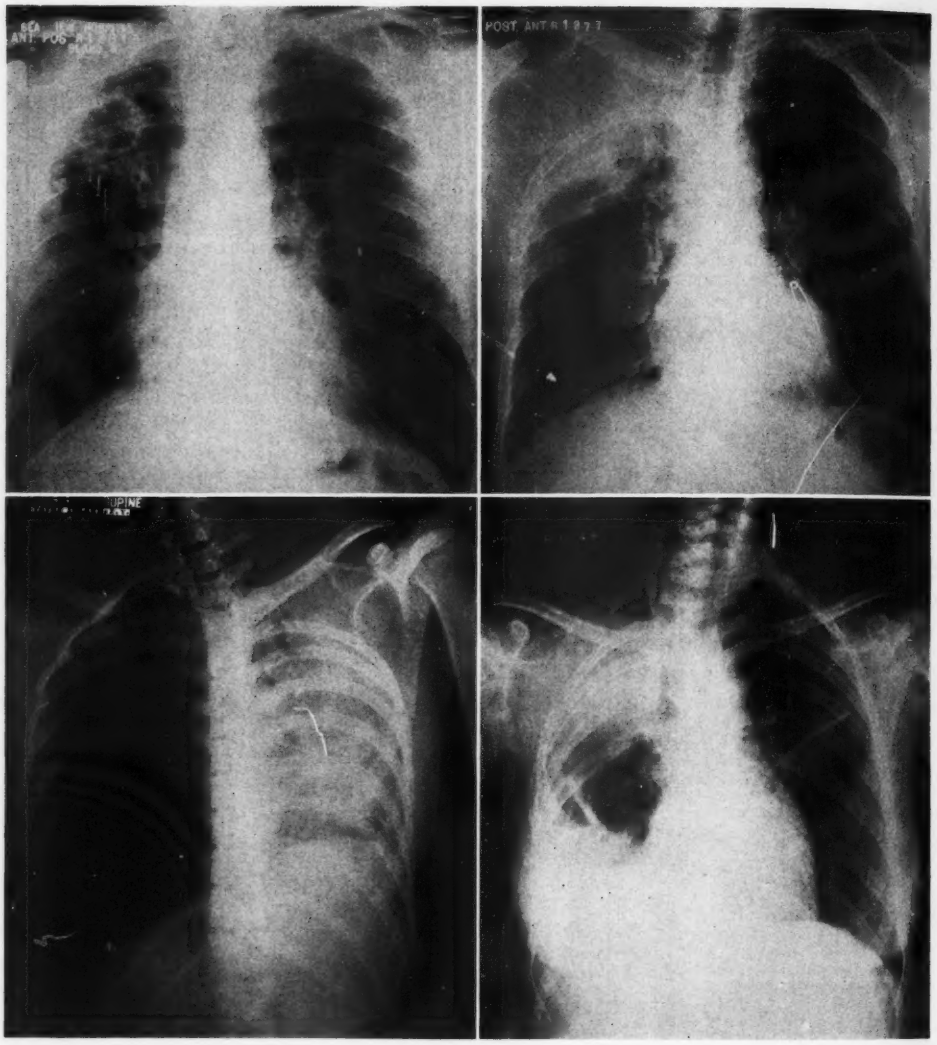

Fig. 5 (*upper left*). Same case as Figs. 6 and 21.
Fig. 7 (*lower left*). Same case as Figs. 19 and 20.

Fig. 6 (*upper right*). Same case as Figs. 5 and 21.
Fig. 8 (*lower right*).

the cavity pre-operatively was relatively large, the lung may be peeled away (decollated) from the surrounding structures, permitting a collapse similar to that of a non-adherent lung. If the lung is decollated farther, the collapse may be even greater than that obtained by the routine thoracoplasty. The mediastinum and diaphragm are not appreciably affected in this stage since there is relatively little pressure exerted on these structures. The displacement of the trachea to the contralateral side depends on its previous position (Fig. 1), its mobility (Fig. 12), and the pressure exerted upon it by the collapsed lung (Fig. 3). If, as a result of pulmonary fibrosis, the trachea is retracted to the affected side pre-operatively, then the collapse of the lung may tend to replace the trachea toward its normal position.

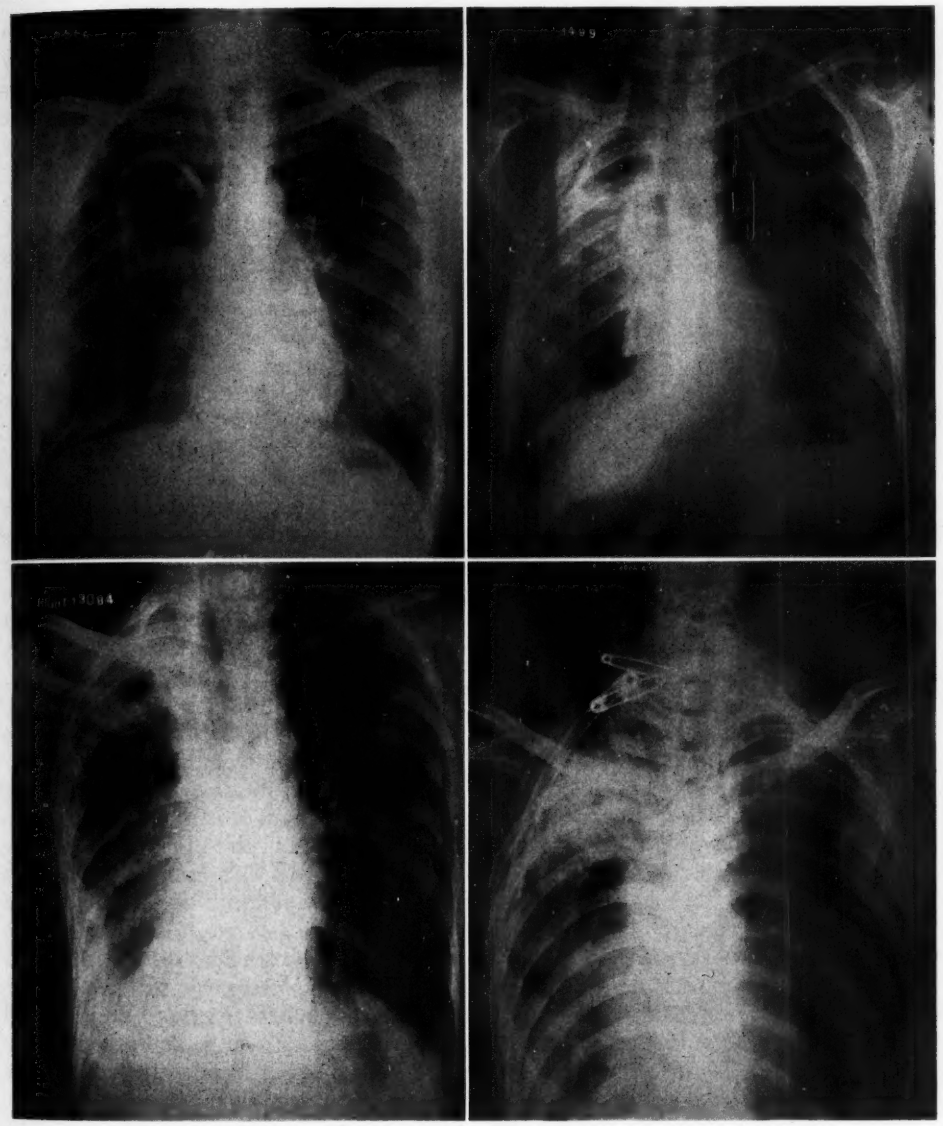

Fig. 9 (*upper left*). Same case as Figs. 10 and 17.
Fig. 10 (*upper right*). Same case as Figs. 9 and 17.
Fig. 11 (*lower left*). Same case as Figs. 12 and 13.
Fig. 12 (*lower right*). Same case as Figs. 11 and 13.

If, on the other hand, it is fixed, its deviation will conform to the displacement of the structure to which it is adherent. The maximum amount of shifting of the trachea is seen generally after the resection of the upper four ribs. The scapula and clavicle on the side operated upon become prominent in this stage (Figs. 3 and 4); but since neither depend on the ribs for support their position and alignment are not appreciably altered by the removal of the ribs. The sterno-clavicular joint on the opposite side appears broadened after the surgical procedure, the result of the rota-

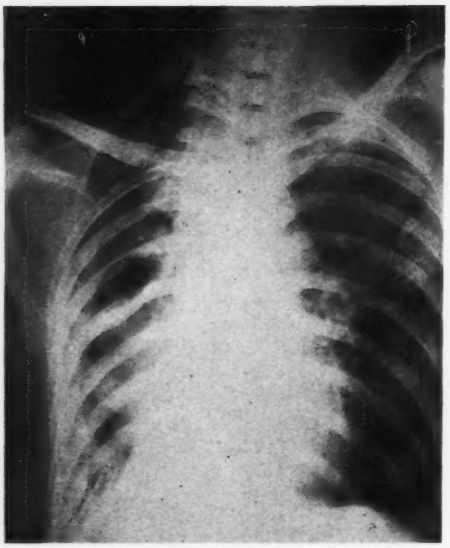

Fig. 13. Same case as Figs. 11 and 12.

tory scoliosis and the anterior displacement of the sternum.

As a result of surgical trauma and the formation of a dead space, air and fluid collect in the soft tissues between the large muscles of the posterior thorax and the extrapleural part of the collapsed lung (Fig. 8). This fluid is generally serosanguinous. The configuration of these collections may vary considerably depending upon the tissues in which they are confined. Air pockets in the wound proper may be confusing and simulate cavitation in the lung (Fig. 1). Only by knowing the previous exact location of cavitation is one able to differentiate between the overlying subcutaneous air pockets, air in the wound, a pre-operative residual pneumothorax, and cavitation in the lung (Figs. 9 and 10, 11 and 12). Frequently dense, sharply circumscribed shadows may be seen in the lateral superior part of the operative area. These shadows may show a fluid level and, therefore, are confused with encapsulated fluid in the pleural space. They are not infrequently diagnosed as localized hydropneumothoracies. At the subsequent operation, this fluid is found localized in the extrapleural tissues and spaces. The overlying gauze dressings and adhesive strappings may also produce additional confusing shadows (Figs. 1, 4, 12); these, however, may be eliminated by the removal of the dressings before the roentgenogram is taken.

Roentgenograms made immediately after the surgical procedure should not be taken as the final result of the partial thoracoplasty (Figs. 12, 13). Changes occur subsequently both in the degree of compression and the degree of aeration of the underlying lung (Figs. 2, 3, 12, 13). Cavitation, which appeared almost completely obliterated in the immediate postoperative study, may become visible after the surrounding reaction has cleared up or the lung has partly re-expanded (Figs. 2, 3). The air in the overlying tissues is usually absorbed after several days, but the fluid in the wound may remain for an indefinite time, and require removal at the time of the subsequent procedure.

SECOND STAGE

Barring contra-indication such as an acute tuberculous spread, atelectasis, spontaneous pneumothorax, or advancement of a contralateral lesion, etc., the second stage is usually performed within three weeks after the first stage. This allows the patient ample time to recuperate from the initial procedure and is early enough to permit intervention before rib regeneration takes place.

In the second stage, the ribs are resected subperiosteally down to and preferably including the seventh rib. Large segments of ribs are resected, beginning as close to the vertebral border as possible and extending well beyond the anterior axillary line. With the vertebral resection of the ribs, occasionally part of the transverse processes are removed.

Roentgenographic studies following the second stage show rough anterior segments of the fourth, fifth, sixth, and seventh resected ribs with the costochondral junction undisturbed (Figs. 14, 18, 20). The transverse processes may or may not be present. The costal structure in the area

above the resection may show early regeneration. The lung at this time is depressed farther downward and mesially toward the hilus, and appears more atelectatic than in the previous stage (Figs. 17, 20, 21). The cavity which was demonstrable before this stage, now appears further depressed and diminished in size (Figs. 17, 20, 21). As in the case of the lung, the cavity is collapsed from above downward, and from without inward toward the hilus. The mediastinum generally shows a shifting to the opposite side (Figs. 14, 18, 20). In left-sided cases particularly, one may also note a rotation of the heart and a change in the contour of the cardiac silhouette. The cusp of the diaphragm is often depressed a full interspace but retains its normal curvilinear appearance (Figs. 14, 18, 20). The position of the trachea is not appreciably altered. The scapula stands out in relief and appears to be displaced farther laterally (Figs. 14, 18, 20). This displacement is most marked when the arm is held in abduction. The clavicle can be visualized in its entirety from the sternum to the acromion. The sternoclavicular joint on the contralateral side shows no change beyond that seen after the first stage. The rotatory scoliosis is now more pronounced and involves a larger segment of the spinal column, frequently extending down to the area of rib resection (Fig. 20). This rotation is again anterior and away from the side of the operation. There is a compensatory curvature in the lower dorsal and lumbar regions, with the concavity toward the operative side. The changes in the wound are similar to those occurring in the first stage. There may be more extensive subcutaneous emphysema and irregular collections of fluid at the site of the operation, and in the surrounding soft tissues. Again, a drainage tube and skin clips may be seen.

As noted above, the second stage is usually performed within three weeks after the first stage. If this stage is delayed further, rib regeneration usually takes place and the resulting collapse of the lung by the routine second stage procedure is relatively inadequate. When new bone is visualized on the roentgenogram, it is too late for a simple second stage procedure. Generally, there is considerably more bone formation than the roentgenogram reveals. In cases in which there has been an unavoidable delay in the second stage procedure, the routine operation should be accompanied by a resection of parts or all of the regenerated ribs. If this delay has been over a long period, it is advisable to resect the regenerated ribs in one stage and at a subsequent date to do a routine second stage procedure. Since the angle of the scapula is at the level of the seventh rib, leaving that rib behind will cause pain as the scapula rides over it. The presence of the seventh rib permits the scapula to become adherent to it by fibrous or bony union, and thereby interferes with the movements of the scapula (Fig. 20). If this occurs, resection of the bony attachment in the third stage may be difficult. The resection of the seventh rib in the second stage permits the scapula to fall in on the soft tissues and also aids the collapse of the lung (Fig. 18).

As a result of the second stage procedure, the apex of the lung usually collapses down to the level of the fourth or fifth rib, with the greater amount of collapse of the lung and cavity from without inward (Fig. 20). The volume of the lung collapsed in the second stage thoracoplasty is usually greater than that in the first stage. As noted in the first stage, further collapse of the lung may be obtained by decollating it from the surrounding adherent tissue.

Due to the mechanical pressure of the collapsed lung on the mediastinum, the latter is usually shifted considerably to the contralateral side (Figs. 14, 18). In cases in which there has been a retraction of the lung and mediastinum to the affected side as a result of chronic pulmonary disease of long duration, the mediastinum will tend to return toward its normal position. In instances in which the mediastinum is not fixed nor retracted, the degree of shift to the contralateral side will de-

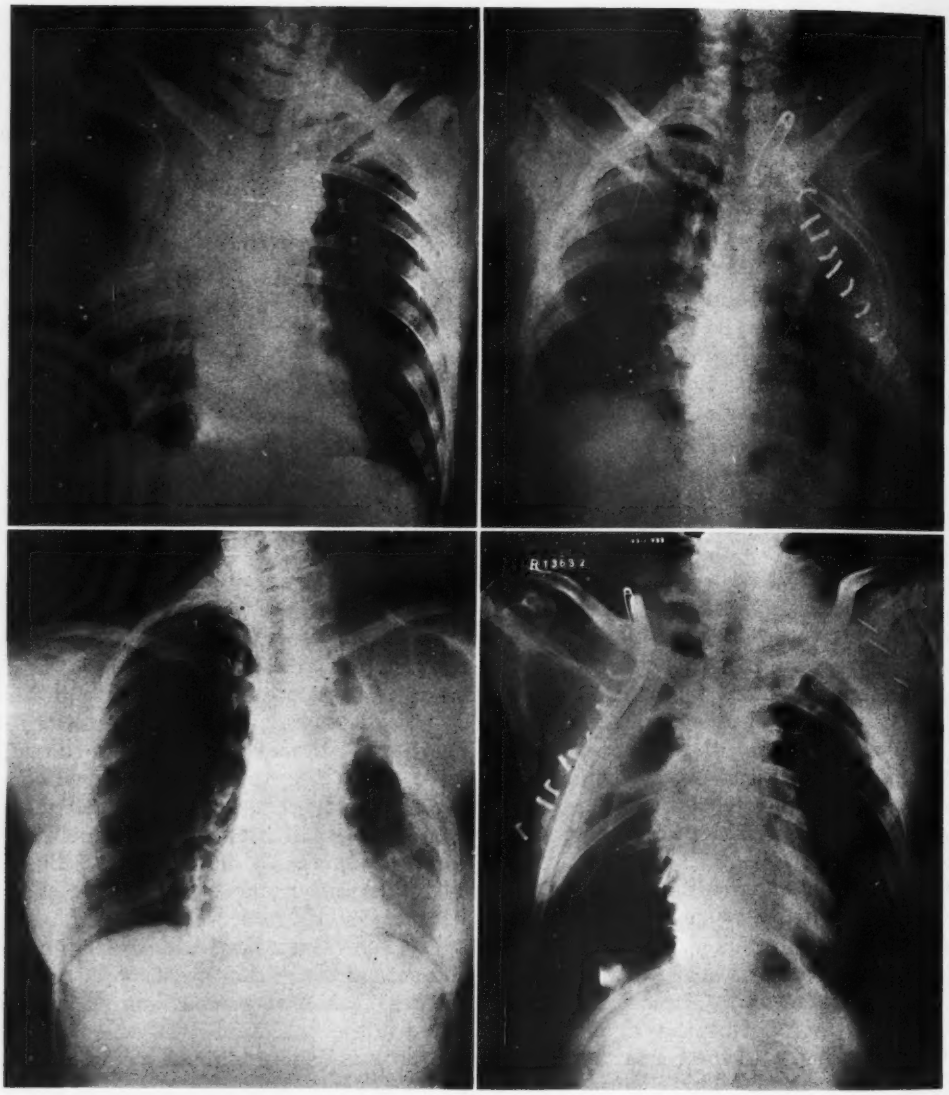

Fig. 14 (*upper left*).
Fig. 16 (*lower left*). Same case as Fig. 15.

Fig. 15 (*upper right*). Same case as Fig. 16.
Fig. 17 (*lower right*). Same case as Figs. 9 and 10.

pend entirely upon the mechanical pressure exerted by the collapsed lung. The rotation of the heart, particularly in cases in which the thoracoplasty has been left-sided, may be so great that it produces cardiac embarrassment. When on the right side considerable embarrassment of the right auricle and superior vena cava may result. The increased pressure exerted within the hemithorax causes the diaphragm to become depressed immediately after the operation. However, this is a temporary state and the diaphragm may later rise to its relatively normal position. At no time is there any impairment of diaphragmatic function. As in the pre-

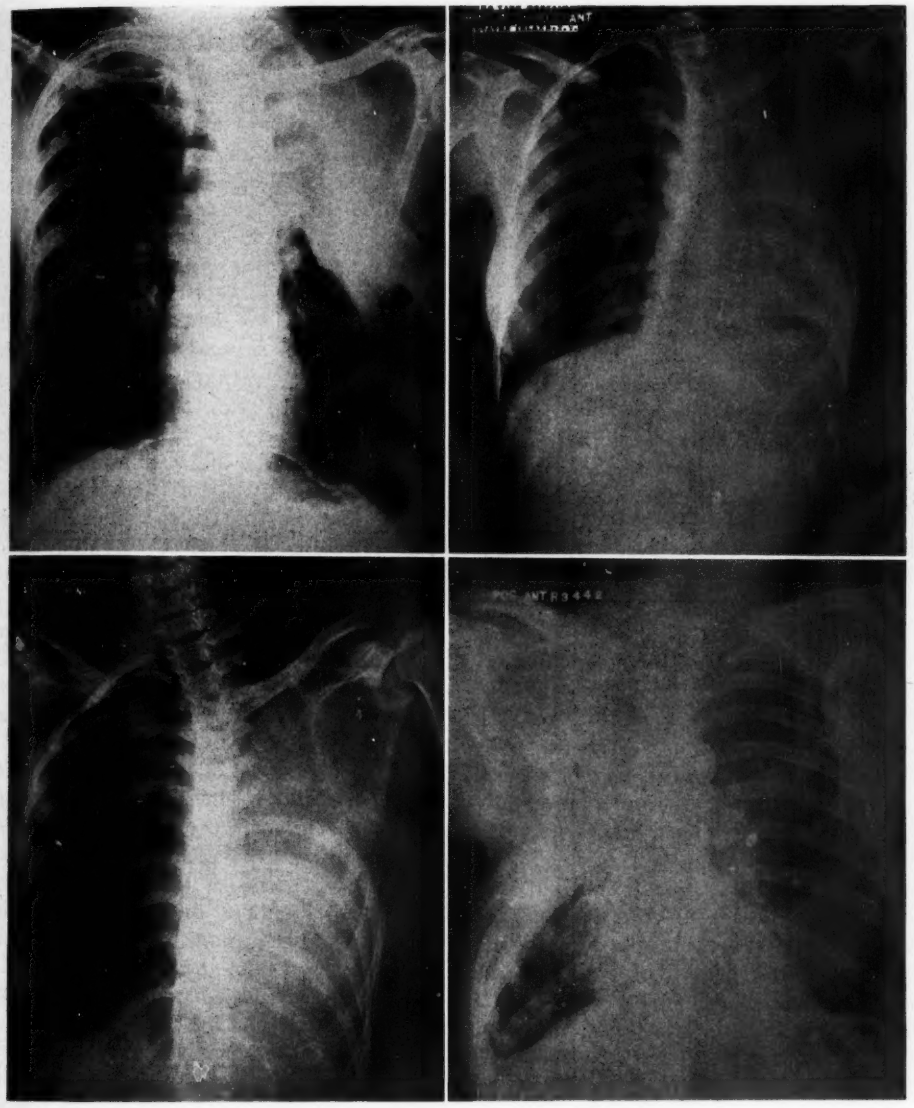

Fig. 18 (*upper left*).
Fig. 20 (*lower left*). Same case as Figs. 7 and 19.

Fig. 19 (*upper right*). Same case as Figs. 7 and 20.
Fig. 21 (*lower right*). Same case as Figs. 5 and 6.

vious stage, roentgenograms taken immediately after the operation should not be considered as the final result of thoracoplasty (Figs. 15 and 16, 19 and 20). Studies made some time after the procedure may show considerable re-aeration of the previously atelectatic lung (Figs. 16, 20). Apparently the lack of visualization of the underlying lung immediately after the surgical procedure is in part due to the reactionary changes in the operative field. With the re-expansion of the lung and absorption of the surrounding reactionary fluid and air, cavitation not previously visualized may become evident. As the lung expands laterally and upward, the

Fig. 22.

mediastinum may be retracted back to the operative side. At the same time, the diaphragm begins to return toward its previous position. As a rule, the lung tissue below the level of the operative field shows no remarkable changes immediately after the operation, but subsequently undergoes emphysematous changes if a third stage is not performed (Fig. 18). The maximum change in the position of the trachea takes place with the resection of the upper four ribs and, therefore, following the first stage. Any further displacement which may take place corresponds to the subsequent mediastinal displacement. No further appreciable pressure is exerted directly on the trachea since the ribs in the first stage were removed down to the level of the corina.

In this stage, with the removal of more ribs, the scapula and clavicle become more prominent and appear further displaced laterally. This change is only an apparent one since actual measurements from fixed bony points to the outer margins of the scapula and clavicle show no appreciable changes. In fact, during the surgical procedure, resuture of the muscles attached to the mesial border of the scapula, brings it back to its relatively normal position. The clavicle and its bony attachments are not disturbed during the surgical procedure. Any changes in position of the clavicle are not due to the operation *per se* but, rather, to changes which have taken place in the structures surrounding the shoulder girdle, as a result of the operation. As in the first stage, the clavicle remains essentially unchanged. Occasionally, however, the clavicle appears elevated or depressed. This is due to the loss of muscular support and loss of antagonistic action of the muscles about the shoulder. The accompanying convex scoliosis and rotation of the spine help rotate the scapula and clavicle anteriorly. With the relaxation of the muscles about the shoulder girdle, the scapula and clavicle may become somewhat elevated or depressed, depending upon which group of muscles remains most unopposed or retracted. The sternoclavicular joint shows no change from that of the first stage. The visualization of this joint is also due to the rotatory scoliosis of the dorsal and cervical spine.

The rotatory scoliosis is more marked at this time, due to the further loss of support by the costal structures and imbalance of the muscular action (Figs. 20, 22). Rotatory scoliosis is the result of the removal of ribs along one side of the spinal column and the unopposed costal pressure on the other side. It is most marked in young subjects in whom the spine is more pliable. It is not infrequently seen in individuals of poor muscular development.

Changes in the wound and surrounding soft tissues are similar to those in the first stage. The air and fluid may again produce confusing shadows. At this time, they occupy a larger area than in the first stage (Fig. 15). The air pockets are most pronounced after the surgical procedure. Frequently, the air and fluid may not be absorbed for a considerable length of time, rendering the interpretation of the underlying pulmonary pathology difficult—in fact, almost impossible (Fig. 18). Not infrequently aspiration of the fluid must

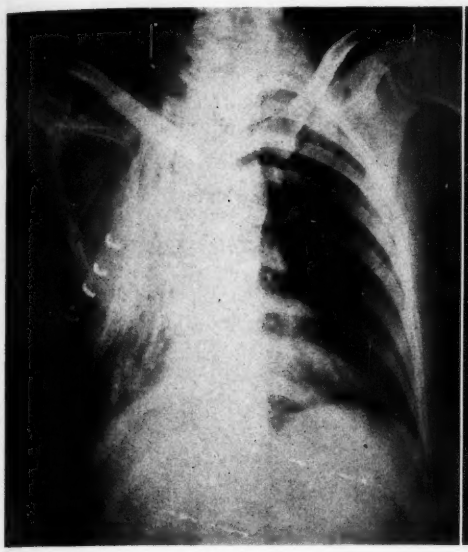

Fig. 23. Same case as Fig. 24.

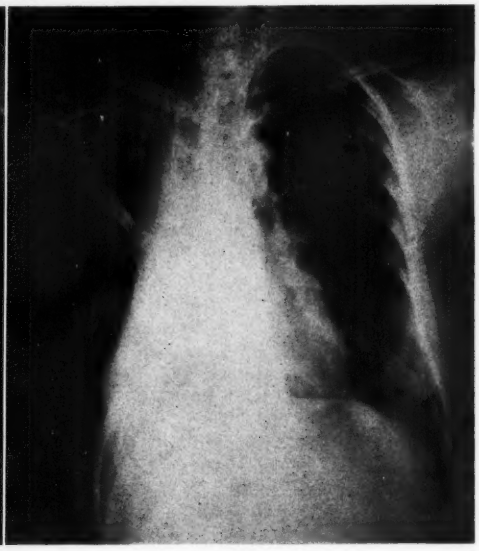

Fig. 24. Same case as Fig. 23.

be resorted to before one can visualize the underlying lung.

THIRD STAGE

The question of whether or not a third stage should be performed depends on the original size of the cavity, its position before thoracoplasty was begun, the persistence of a positive sputum after the second stage, and whether or not there are other contra-indications such as those mentioned in the introduction to the second stage. If a third stage is contemplated, namely, the removal of ribs down to and including the tenth or eleventh, it should be performed before rib regeneration becomes a definite handicap to the collapse of the lung. If the delay is longer it requires the removal of regenerated ribs, which is difficult and not without danger. The ribs in this stage are again removed subperiosteally, as in the first and second stage, leaving the costochondral junction undisturbed and the anterior portions of the ribs in place.

On the roentgenogram, there is evidence of removal of the lower costal structures with the anterior portions of the ribs remaining *in situ* (Figs. 23, 26). As a rule, these remaining stumps are longer than those in the first and second stages. The transverse processes in the lower cervical and upper dorsal regions being longer than those in the lower dorsal region, gives one the impression that longer posterior costal segments have been left behind in the upper dorsal regions than in the lower, although the ribs throughout were resected as close to the vertebral articulations as possible. The lung appears to be collapsed laterally. In cases in which a cavity was visualized pre-operatively, the compression appears laterally, corresponding to the collapse of the surrounding lung tissue (Figs. 23, 24, 27). The mediastinum is generally shifted considerably to the opposite side (Figs. 26, 27). The trachea in this stage is not affected by the collapse of the lung except where it is the result of general displacement of the mediastinum (Figs. 26, 27). The diaphragm appears markedly depressed and flattened with its sides standing almost in the erect position (Figs. 26, 27). There is a more pronounced curvature and rotation of the dorsal spine with compensatory changes

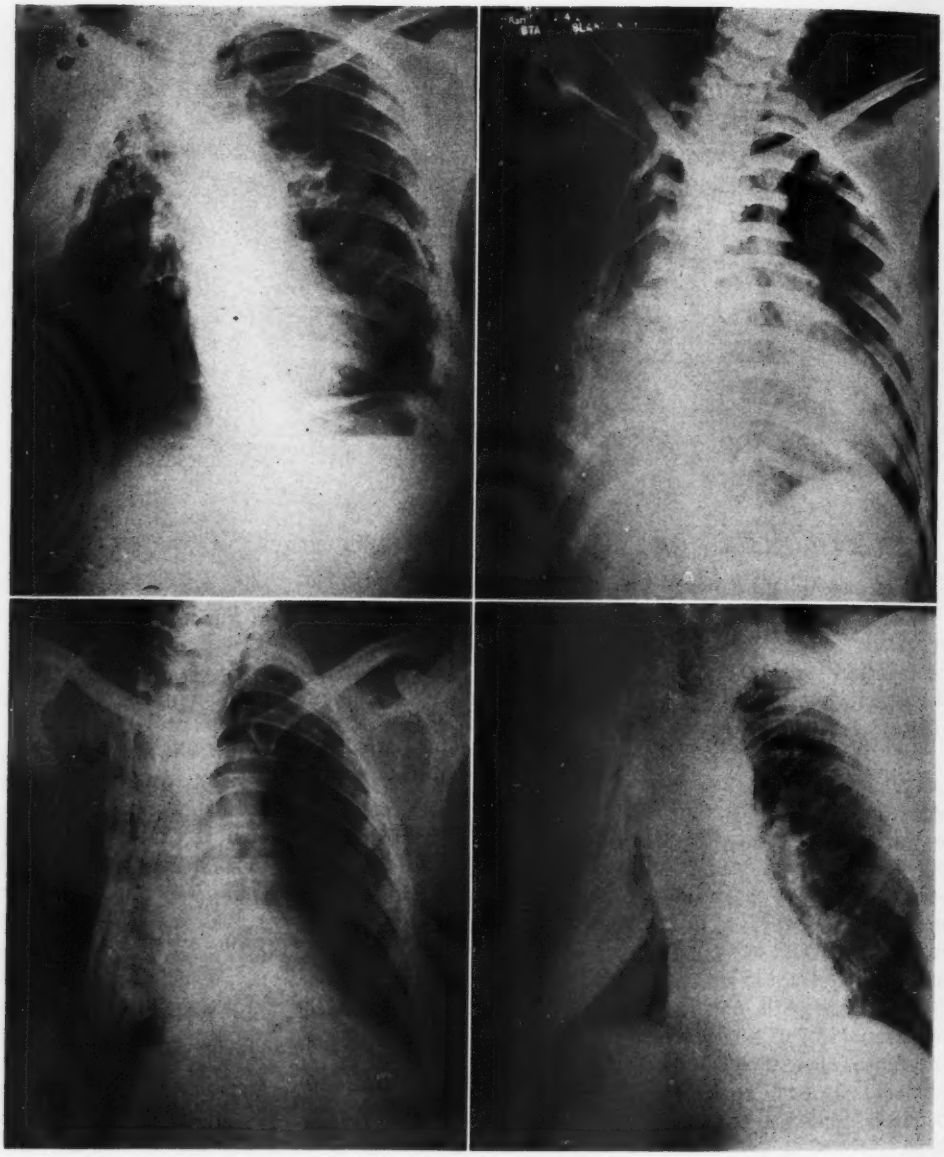

Fig. 25 (*upper left*).
Fig. 27 (*lower left*).

Fig. 26(*upper right*)
Fig. 28 (*lower right*).

in the cervical and lumbar regions (Figs. 26, 27, 29, 30, 34). The findings in the wound are similar to those in the first and second stages but less extensive.

In cases in which the cavity was originally large even though it appears obliterated by the routine two-stage thoracoplasty, a third stage is deemed advisable. On the other hand, in cases in which the cavity was small and the sputum remains persistently negative, a third stage as a rule is unnecessary. In those in which the cavity was originally small and a two-stage procedure has been performed but

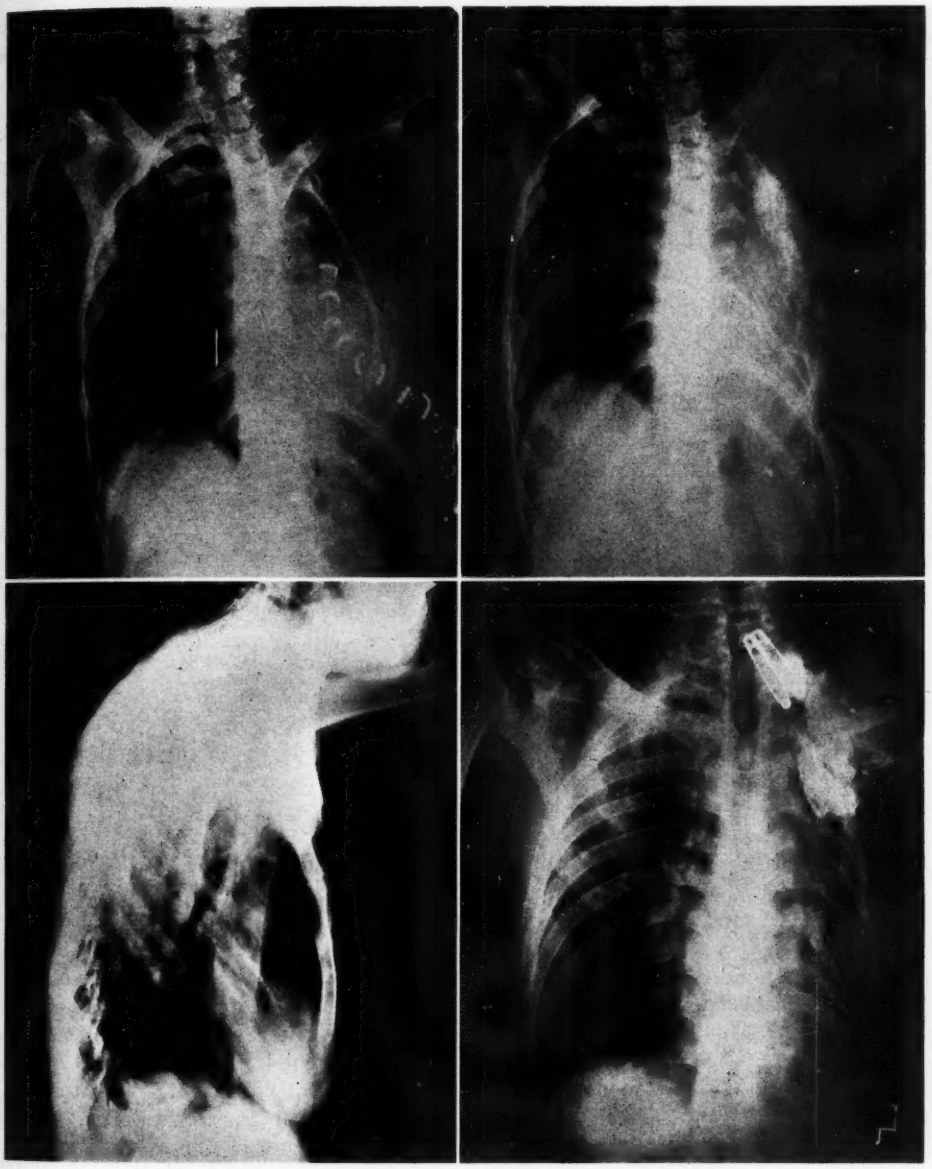

Fig. 29 (*upper left*). Same case as Fig. 30.
Fig. 31 (*lower left*).

Fig. 30 (*upper right*) Same case as Fig. 29.
Fig. 32 (*lower right*).

has failed to yield a persistently negative sputum over a period of several months, a revision operation is advisable rather than a third stage. In cases in which there is a caseous pneumonic lesion in the contralateral lung, a third-stage procedure on the original side, if contemplated, should be withheld until the contralateral lesion is controlled (Fig. 25). This permits one to increase the degree of collapse on the contralateral side with less respiratory embarrassment.

In the third-stage thoracoplasty the downward collapse of the lung is mini-

mal, the collapse being almost entirely from without inward. Compared to the first and second stages there is less depression of the lung and cavity and less atelectasis (Figs. 23, 24). As a result, only that pathology located toward the periphery of the lung and not adherent high up, will be appreciably affected. The third-stage procedure is of little benefit in cases in which the original cavity was located in the apex of the lung and failed to drop following the first and second stages. In such instances, a radical revision of the upper regenerated ribs is necessary. Before this is undertaken, roentgenographic studies are made for the location and position of the uncollapsed cavity, and from these studies the course of the revision is planned. Here, usually, regenerated and previously unresected ribs are removed. Considerable cartilaginous regeneration may be present which is not visible on the roentgenogram, so that the extent of the surgical procedure cannot always be judged until the operation is being performed. The surgical procedure is usually greater than the roentgenogram would indicate. This revision operation may follow any stage, whenever the surgeon feels that the results of the previous procedure are unsatisfactory. Frequently, in addition to this revision, pressure is necessary to collapse a large thick-walled cavity. This may be obtained by means of a pressure packing applied outside of the pleura against the decollated lung (Figs. 29, 30, 32).

In this stage, the mediastinum is shifted to the contralateral side much more than in the first and second stages, the result of greater lateral pressure exerted by the collapsed lung. The displacement of the mediastinum will depend on its mobility and the number of ribs removed. Accompanying this shifting there is further rotation of the heart (Figs. 26, 27). With all these changes there is an increased pressure in the narrowed hemithorax and as a result the diaphragm becomes further depressed and flattened (Figs. 26, 27).

In addition to the scoliosis usually seen in this stage, there may be an accompanying kyphosis, due in part to the loss of muscular support of the spine and in part to the post-operative posture of the patient. The deformity may become permanent as a result of bony regeneration of the ribs, fixing the spinal column in that position. Early corrective exercises are necessary to prevent gross spinal deformities. The prominence of the sternum at this time (Fig. 31) is the result of the removal of the ribs on one side and the rotatory scoliosis. The findings in and about the wound are essentially the same as in the previous two stages, but being a relatively simpler procedure, there is less surgical trauma and therefore the changes in the tissues are less pronounced.

After the completion of the thoracoplasty bony regeneration takes place in the area of resected ribs, the end stage of which is the formation of an irregular bony, hard plaque (Figs. 26, 34). The direction of regeneration bears no relationship to the original position of the costal structures. This bony wall forms a dense cage on the outside of the parietal pleura to which the periosteum was left adherent at the time of the subperiosteal resection of the rib. The regeneration of the ribs as seen on the roentgenogram gives an indication of the direction the pleura has taken in its collapse following thoracoplasty (Figs. 26, 27, 32, 34). Some time after the completion of the thoracoplasty the mediastinal structures are pulled back toward the operative side by fibrotic contractions in the lung. However, the mediastinum is not completely reposited in its normal position (Figs. 24, 28, 32). It may be retracted toward the affected side to a varying degree.

Thoracoplasty not infrequently follows an unsuccessful pneumothorax, *i.e.*, in cases in which pneumothorax has failed to collapse the diseased area. The presence of air in the pleural space at the time of surgical intervention interferes with the collapse of the lung by thoracoplasty, by preventing the coaptation of the parietal and visceral pleuræ. If this

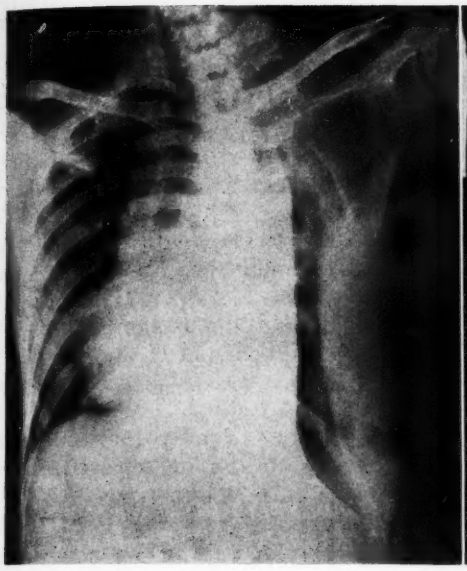

Fig. 33.

Fig. 34.

air is not aspirated the parietal pleura with its adherent costal periosteum is held out in the semi-collapsed state. As a result of rib regeneration, this position becomes permanent, unless completely revised. With the absorption of the pneumothorax the lung re-expands, filling the pleural space, thereby defeating the purpose of the thoracoplasty.[2] The re-expansion of the lung is indicated on the roentgenogram by a bulging of the upper lateral chest wall (Figs. 29, 30, 33).

The routine thoracoplasty produces a general narrowing of the chest with retraction of the tissues to the affected side. The entire hemithorax assumes a triangular configuration with the base toward the diaphragm. The contralateral lung becomes emphysematous and hypervascularized (Figs. 24, 27, 28).

Routine anteroposterior and posteroanterior roentgenographic studies of the post-thoracoplasty chest do not always give all the information about the thorax that it is possible to obtain. In cases in which additional information is desired various alterations in technic may be used, such as (1) the over-exposed or Bucky film to demonstrate the condition of the collapsed lung; (2) the method of Sampson and Gershon-Cohen in which a double exposure is obtained on the same film, producing an over-exposure of the side operated upon and a normal exposure on the side not operated upon, and (3) the stereoscopic roentgenogram to help separate otherwise confusing shadows.

[2] The subject of thoracoplasty in the presence of pneumothorax will form the basis of a subsequent communication.

201 Linden Boulevard (L. A. H.)
700 Ocean Avenue (L. N.)

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SHOULD THE METHOD OF COUTARD BE APPLIED IN ALL CASES OF CANCER TREATED BY ROENTGEN RAYS?[1]

By W. EDWARD CHAMBERLAIN, M.D., *and* BARTON R. YOUNG, M.D., *Philadelphia*

From the Department of Radiology, Temple University Medical School and Hospital

THE Coutard method is based on the observations of Regaud (1), who found that a single dose of x-rays sufficient to sterilize a rabbit's testicle produced severe skin and tissue destruction, but if this same total dose of x-rays was administered in small fractions, over a number of days, sterilization was produced without significant effect on the skin and subcutaneous tissue. Coutard (2) utilized this knowledge in the treatment of cancer and evolved an entirely new principle, that of administering a large total dose of x-rays to a tumor by giving small fractions of the total dose daily over a long period of time in days. Although the dose was sufficiently large to either partially or completely sterilize the tumor, the integrity of the skin, subcutaneous tissues, and blood vessels was not seriously impaired.

Roentgen therapists who apply the method of Coutard should not be expected to adhere to a rigid technic since the originator of the method follows none. The system used by Coutard (deciding twice per day what field size and dose to apply) is unscientific. The condition visualized at any given observation is the result not of the most recent radiation (six to 24 hours before) but of the treatment or treatments many days previously. We believe it is much more scientific to lay out a plan of therapy at the start, based upon location, size, microscopic appearance, and presence or absence of complications, and then adhere as closely as possible to it. Coutard learned that it is necessary to destroy the superficial epithelium and from experience decided that the daily fractions must be continued for from 20 to 40 days, depending upon histologic nature, location, and size of the tumor. Many of the patients were treated twice daily, in the morning and afternoon. The technical factors employed by him are as follows: low milliamperage, 4–5; low intensity, from 2.5 to 4 r per minute; heavy filtration, 2 mm. Cu plus 2 mm. Al; 50–70 cm. target-skin distance, and approximately 200 kv.p. (the kv.p. was less in the earlier years of study).

It is interesting to study the innumerable modifications, there being almost as many technics as radiologists. However, in a general way those who use Coutard methods can be placed in one of two large groups, *viz.*, those who attempt to follow the method rather rigidly and those who have accepted the principle but modify the technic to suit their individual needs. Since we ourselves belong to the former group we feel that we are in a stronger position to point out superstitions and separate them from facts. Such an attempt by one who has been using a modified Coutard technic might be considered as a defense of his method rather than an unbiased analysis. Much emphasis has been placed on the advisability of using low intensity (not more than 5 r per minute), highly filtered (2 mm. Cu) x-rays, but although we ourselves have strictly adhered to this part of the technic, we know that comparable results have been obtained with a high intensity, inferiorly filtered (0.5 mm. Cu) beam. The splendid results obtained at the Memorial Hospital, of New York City, in treatment of cancer of the larynx and hypopharynx, with high intensity, 0.5 mm. Cu filtered x-rays, and the experimental work of McWhirter (3) indicate that these two factors may be varied. We ourselves believe that the essential factors in the method of Coutard are (1) frequent (for example, daily) doses of relatively small fractions and (2) protraction as stated above, until covering epithelium is lost.

[1] Read at the Twenty-second Annual Meeting of the Radiological Society of North America, at Cincinnati, Nov. 30–Dec. 4, 1936.

While scientific reasons can be advanced for a belief in the importance of other factors (*e.g.*, target-skin distance of not less than 50 cm. and kv.p. of not less than 200), the indications are that some variation in these factors is permissible.

Since the results of Coutard therapy in treatment of cancer of the larynx, pharynx, and hypopharynx have been so far superior to any present or previous method, no other procedure should be considered when x-ray treatment for the disease in this location is indicated. The same statement holds for cancer in certain other organs, for example, cervix, breast, bladder, esophagus, bronchus, and rectum, although it is often necessary to modify the dosage depending on size and location of the tumor and condition of the patient.

Let us now consider the possibility that there may be special types of tumor in which results from Coutard therapy may be inferior to results with single massive doses or some other technic of radically different type. It has always been obvious that in those lesions which respond to Coutard therapy better than to "massive doses," the advantage of the protracted fractional dose method must rest upon the existence of a more rapid "recovery rate" in the skin than in the tumor. In other words, if the cells of a tumor are able to recover from the effects of radiation more rapidly than the cells of the overlying skin, the net result of protraction will be a loss. There will be a greater accumulation in the skin and a relatively less pronounced effect in the tumor.

Theoretically there is reason to suppose that cells with relatively high metabolic rates will exhibit relatively rapid rates of recovery from toxic effects, including the effects of radiation; furthermore, that cells undergoing very rapid mitosis tend to have elevated rates of metabolism. On such theoretical grounds as the above one expects to find at least an occasional, very rapidly growing neoplasm which merits treatment by a massive single-dose technic.

Turning now from theory to practice, we may cite the case of Mrs. W., who received a protracted fractional dose series in June, 1931, and a short, more intensive three-day series three months later. Her rapidly growing lymphosarcoma of the tonsil regressed only partially after the first (protracted fractional) series, resumed rapid growth in September and regressed rapidly and presumably completely after the short intensive series. Three years later when she died a cardiac death, this patient was still apparently free from recurrence of her tumor. It is our conviction that were we more often in a position thus to compare the relative efficiencies of "protracted fractional" and "massive dose" technics, in the same patient and for the same tumor it would soon become a matter of common knowledge that there are tumors requiring massive doses just as surely as there are tumors that require the method of Coutard.

(In a consideration of the indications for a "massive dose" method, it should be remembered that certain very small superficial growths are completely destroyed by a single large dose of from 3,000 to 5,000 r, with complete assurance that the resulting ulcer, of small size, will completely heal. An example would be a small or moderate sized, isolated nodule of recurrent breast cancer in an accessible or superficial location. Such a lesion would undoubtedly respond well to Coutard therapy, but considerations of justifiable economy and common sense dictate the use of a large single dose.)

In the foregoing discussion we have cited tumor types which require "protracted fractional" methods (slow growing tumors, mostly of epithelial origin), and tumor types which, in our opinion, require a "massive dose" technic (certain highly anaplastic tumors such as a very rapidly growing lymphosarcoma of the tonsil). Are there perhaps still other technics, particularly applicable to certain special tumor types not included in the above groups? We believe that there is at least one such.

In the past we have been impressed by the very serious damage which occurred in the skin and subcutaneous tissues of certain

patients. Strangely enough, these patients were not the ones who had received large individual doses or repeated daily fractions with high total dosage. Analysis of their records revealed that they had received either small or moderate doses at weekly, bi-weekly, or monthly intervals for many months. It was quite apparent that this type of radiation had been more damaging to the blood supply than any other type. The question now arises as to whether this tendency (for an interval of about one month between treatments to destroy or diminish the blood supply) may be put to clinical use. Our own experience indicates that it can, and we give serious consideration to a plan of monthly doses of from 300 to 800 r (usually in a three- or four-day series) whenever we are faced with (1) a highly radioresistant tumor and a histology that indicates a high degree of tissue differentiation (examples—fibrosarcoma, neurofibroma, metastasizing thyroid adenoma), or (2) when the element of vascularity is an important factor (examples—hemangioma, certain telangiectatic tumors of the spinal canal, some highly vascular but relatively radiation-resistant sarcomas of bone). While the literature appears not to contain any analytical allusions to this type of technic, it is obvious that Newcomet (4), Ewing (5), Ginsburg (6), and others have consciously or subconsciously adopted some such method.

Entirely aside from the fact that attempts to apply the method of Coutard to all tumors are bound to result in depriving at least an occasional case of a more fitting type of treatment, there is a further reason for avoiding the large total dose and violent reaction of a Coutard series, except when the indications for same are quite definite. We refer to the danger that serious skin lesions may develop, in the distant future, if not sooner. An indication of the remarkable latency of some of these late roentgen catastrophies is to be seen in the following case history.

Case Reports.—R. S., white male, aged 46 years, received x-ray therapy over his face for acne, in 1910, at the age of 20 years (26 years ago). During the ensuing 20 years he had no reason to suspect that he had suffered injury. In retrospect he now realizes that he needed to shave only about twice per week, while his friends found it necessary to shave daily. Nevertheless, his first inkling of trouble came in 1930 when a friend called his attention to a certain "pinched look" about his nose and chin. Between 1930 and 1935 he progressively developed atrophy, telangiectasia, and multiple epitheliomas that have necessitated plastic surgery of an extensive type. Our reason for citing this admittedly very unusual case is to call attention to the possibility that skin lesions more serious than we now anticipate, may be in store for us in those cases that may be destined to live 20 or more years after they have undergone a Coutard series. Such a possibility would seem to contra-indicate the use of such a radical method of treatment except in cases in which the indications are quite definite and the condition in need of treatment a serious one.

SUMMARY

The two essential factors in the method of Coutard are (1) frequent (for example, daily) doses of relatively small fractions, and (2) protraction until a very large total dose has been administered. Within certain limits such other factors as target-skin distance, voltage, filter thickness, and r-afflux (r per minute) are non-essentials or objects of superstition rather than accurate knowledge.

The method of Coutard is so far superior to other forms of roentgen therapy in certain cancers that the use of any other method is inconceivable. Despite this fact, any attempt to apply it universally in the x-ray treatment of malignancy is a serious mistake. Intelligent treatment is based upon individualization, with careful attention to such factors as size and location of tumor, histopathology, and general condition of patient. In the present paper we have cited instances of tumors that require treatment by the single massive dose

method and other tumors that are certainly resistant to either the massive dose or the Coutard method, yet may respond favorably to a special type of irradiation consisting of moderately large doses (usually in the form of a three- to four-day series) at (approximately) monthly intervals.

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INTERLOBAR EFFUSION ASSOCIATED WITH HEART FAILURE[1]

By JOSEPH LEVITIN, M.D., Roentgenologist, Mount Zion Hospital, *San Francisco*

INTERLOBAR effusion is associated in the minds of most general practitioners with infection in the lungs. The usual source of infection is pneumonia, lung abscess, or tuberculosis. That it can occur as an aseptic effusion has been recognized by a few observers. A common cause of aseptic effusion which should be kept in mind by those interested in diseases of the chest is an effusion occurring with cardiac failure.

lobar effusion in a case of cardiac failure. The heart disease was a primary atherosclerosis. The effusion disappeared with recovery of the patient and reappeared with the subsequent cardiac failure. The accumulation of the fluid was a primary pleural process and was due to previous obliteration of the peripheral pleural cavity, leaving the interlobar space as the only one into which transudation could occur.

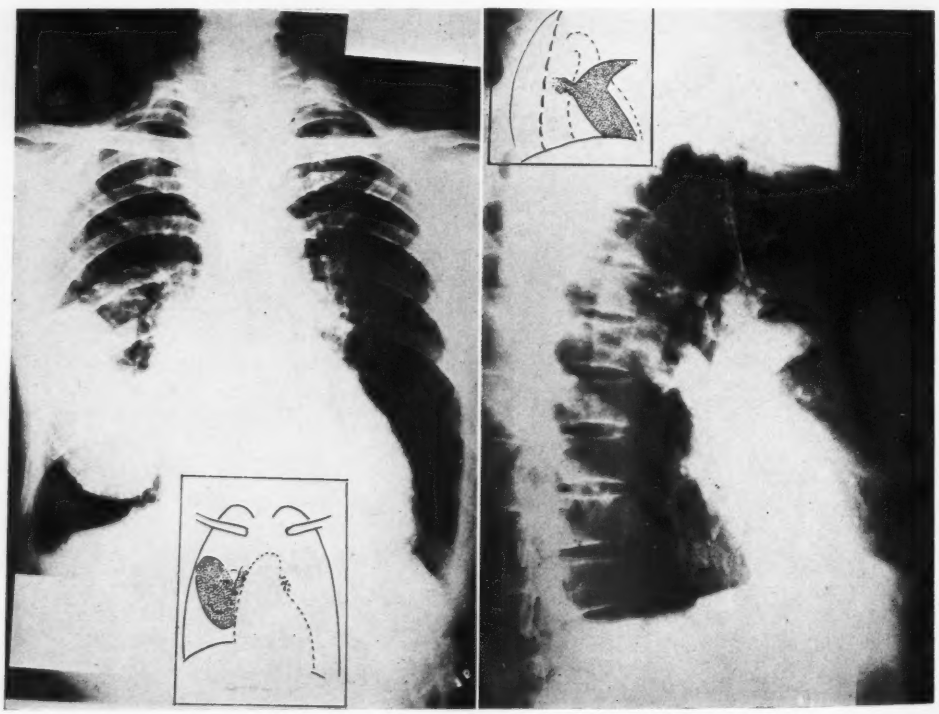

Fig. 1. Interlobar effusion between the lobes on the right side.

Stewart (1), in 1928, was the first to describe the occurrence of encapsulated inter-

In addition to this case of Stewart's, Kiser (2), in the next year, reported a case of myocardial failure with congestion. Steele (3), in 1931, reported two additional cases in which interlobar fluid appeared, in the right upper half of the chest, with

[1]From the Department of Roentgenology, Mt. Zion Hospital, and the Department of Surgery, Division of Thoracic Surgery, University of California Medical School, Service of Dr. Brunn.

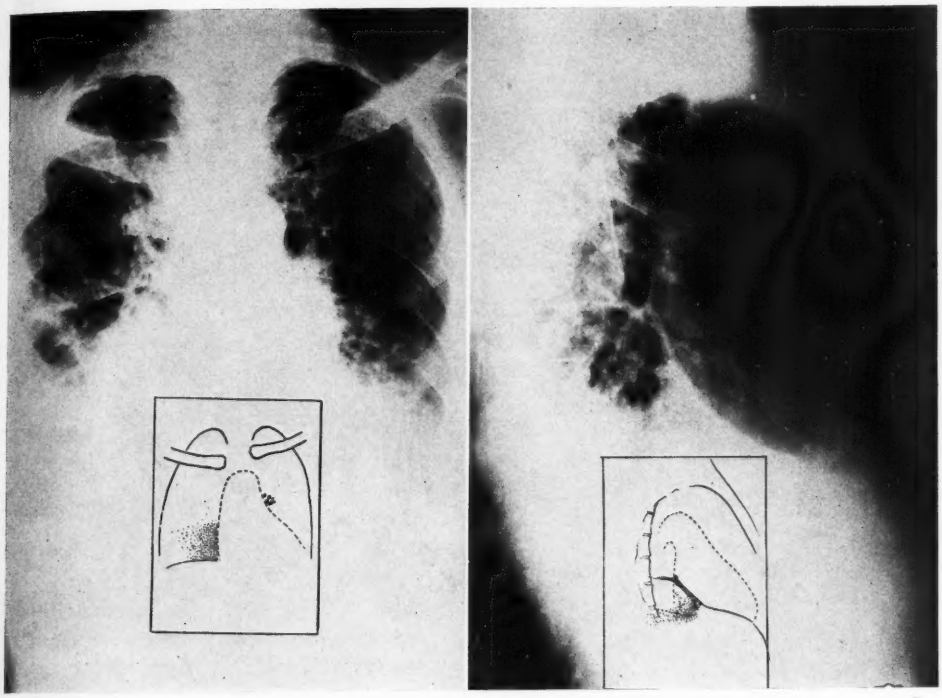

Fig. 2. Interlobar effusion between right middle and lower lobes. Pleural effusion right base.

recurrent attacks of heart failure, and disappeared with the disappearance of the edema and with general recovery. These shadows reappeared with the second attack. One case came to autopsy and showed obliteration of all pleural spaces except the one between the upper and middle lobes, where 250 c.c. of fluid was found. For the effusion to be limited to the interlobar space, Steele concluded that extensive adhesions are necessarily antecedent to the development of the heart failure.

In 1931, Freedman (4) reported a case of effusion between the right upper and middle lobes. This patient had a coronary occlusion and an aneurysm of the left ventricle. Freedman emphasized the fact that interlobar effusion must be differentiated from localized marginal pneumonia and bronchial carcinoma. He further stated that in the presence of a pneumonia the only x-ray sign of interlobar effusion is a bulging of the interlobar fissure seen in the lateral view.

Austrian (5), in 1932, reviewed the literature and added his own case which showed an interlobar effusion during periods of congestive heart failure. At postmortem there was found an antecedent obliterative pleurisy, probably of tuberculous origin, so that the interlobar space was the only one in which the fluid could accumulate. All of the cases he reviewed had coronary disease or disease of the aorta near the ostia of these vessels. The fluids found were all on the right side.

Stein and Schwedel (6), in 1934, stated that interlobar effusion in patients with cardiac failure is not uncommon. The cases they described also occurred with pleural effusion.

Rigler (7) reviewed 18 cases with interlobar effusion, which were all right-sided, and concluded that in heart disease it may arise as an exudate from a pleurisy or

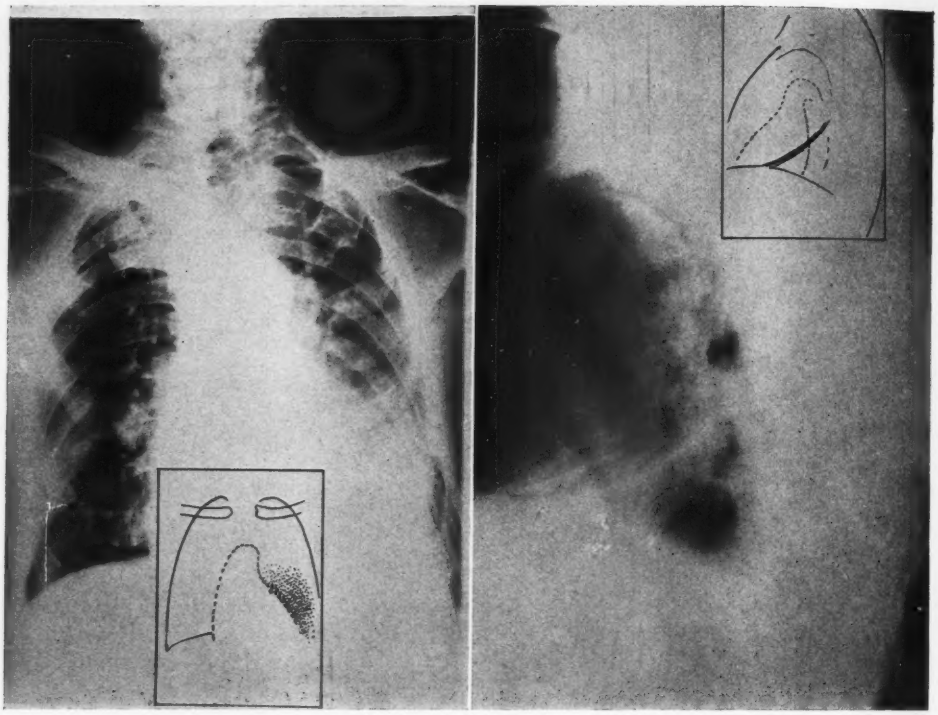

Fig. 3. Interlobar effusion on left side. Encapsulated effusion in right axilla.

pericarditis in the course of active rheumatic fever, following an infarction along a pleural surface, or during cardiac decompensation. This results in a transudation from congested lungs and pulmonary stasis. In these cases there were no preceding histories of pneumonia or pleurisy, but it was thought that during cardiac decompensation and repeated bouts of failure, pleural reactions occur which lead to thickenings. The interlobar pleuræ are least affected by the thickenings because pleurisy is more common between the visceral and parietal pleuræ, spreading rapidly with respiration. Drainage of the interlobar pleura is facilitated by two areas of lung surfaces, while the pleural cavity has a rigid chest wall and only the visceral surface for absorption. Fluid also gets into the interlobar space by seepage from the general pleural cavity.

Shiflett (8) discussed the subject, added two cases to the literature and emphasized the lack of clinical symptoms. He warned against confusing these shadows with metastatic malignancy.

The diagnosis of interlobar effusion is facilitated by an x-ray in the postero-anterior and lateral views. In the postero-anterior view the appearance of the interlobar effusion will depend upon the fissure in which the effusion occurs. In a previous article (9) we demonstrated the appearance of effusions occurring in the different fissures and found that broad shadows are obtained by effusions along the oblique longitudinal fissure bordering the lower lobe and a narrow band shadow if the effusion occurs between the upper and middle lobes. The lateral view is most important in differentiating this shadow from either a pneumonic consolidation or general effusion in the pleural cavity. In this view a definite band or shadow of elliptical shape, depending upon the amount of effusion, will be clearly demonstrated.

There is no doubt but that interlobar effusion is more common than is usually recognized, as it may be masked by a general pleural effusion.

In reviewing our series of interlobar effusions, we have found three cases which were the result of cardiac decompensation.

CASE REPORTS

H. K., a male, 51 years of age, entered the service of Dr. Kerr, at the University of California Hospital, suffering from marked dyspnea, orthopnea, and cyanosis. He had a positive blood Wassermann. Physical examination showed fluid in the left chest. Heart: Apex beat in the fifth interspace, 12 cm. from the midsternal line. He had a diastolic and a systolic murmur over the aortic area, moderately sclerotic peripheral vessels and a Corrigan type of pulse with marked capillary pulsation. Blood pressure was 220/30 in the left arm and in the right arm 180/30. X-ray examination showed interlobar effusion between the lobes on the right side and fluid in the left chest. Under treatment of digitalis, digifolin, caffeine, and thorocentesis he improved and was discharged. He re-entered one month later with the same symptoms and re-accumulation of fluid. On the second entry there was a gradual increase in aortic insufficiency with resulting cerebral anoxemia and mental changes. He died following an accident and at autopsy fluid was found in the left chest, and the right pleural cavity was obliterated by dense fibrous adhesions. Encapsulated fluid was demonstrated in the interlobar fissure and also some at the base.

L. C., aged 57, entered Mt. Zion Hospital on the service of Dr. Briggs, with the complaints of dyspnea, orthopnea, and edema of the extremities. A diagnosis of arteriosclerotic heart disease with decompensation and auricular fibrillation was made. X-ray examination of the chest showed fluid at the right base and between the middle and lower lobes. With bed-rest and digitalis medication the edema cleared, the fluid disappeared, and the patient left the hospital.

H. F., aged 74 years, entered the service of Dr. Briggs at Mt. Zion. This patient complained of a progressive dyspnea on exertion for the past two years. He entered with physical findings of cardiac failure, edema of the extremities, and a heart enlarged to the left. X-ray showed interlobar effusion on the left side and encapsulated in the right axilla. With digitalis and rest the effusion cleared in two days.

CONCLUSION

As one of the causes of interlobar effusion one must keep in mind that of heart failure. If there is an obliterative pleuritis, the effusion will occur only between the lobes. This fluid disappears with the general improvement of the patient and does not require any specific therapy other than treatment of the decompensation. Roentgenograms should be taken in the posteroanterior and lateral positions. The lateral position is most important, as it is in the plane of the fissure. The appearance of the effusion within the fissure may be in the form of a band or ellipse, depending on the amount of the effusion.

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AN ATTEMPT TO INVOLUTE COMPLETELY ALL OF THE LYMPHOID TISSUE OF THE ALBINO RAT BY X-RAYS

By CHARLES W. HUGHES, M.S.,M.D., *and* THESLE T. JOB, PH.D., *Chicago*

From The Department of Anatomy, Loyola University School of Medicine

IRRADIATION of the thymus has been resorted to by clinicians for the past twenty years to correct respiratory stridor in infants, and it has been done as a pre-operative procedure when respiratory difficulties were present. In the course of such treatment, some clinicians have observed deleterious effects (5), while others have observed no injurious effects (1, 7). Observations of the results of thymectomy have been extensive and productive of controversy (8). Is there a correlation of function of the thymus gland and other lymphoid tissue including the tonsils, lymph nodes, and spleen? Are the results of thymectomy so indefinite because the remaining lymphoid tissue supplants the thymus gland? The answers to these and many other similar questions have not been completely demonstrated.

In 1927 Wintz (11) used x-rays to destroy the germinal epithelium in ovaries without apparently injuring other ovarian tissues. In 1926 Tsuzuki (10) found that the lymphocytes, lymphoid tissue, thymus gland, and testes of the rabbit were sensitive to x-rays in the sequence indicated. These facts made it seem possible that small doses of x-rays should destroy at least a major portion of all the lymphoid tissues, including the thymus gland, without detrimental effects to other tissues. If an animal with no lymphoid tissue and all other tissues normal could be prepared and observed, the results should be interesting.

Consequently, the object of this research was to cause by means of a definite dose of x-rays a differential involution of all, or as much as possible, of the lymphoid tissues of albino rats and then to observe the effects of such an involution on the growth, development, and subsequent physiologic behavior of the rat. We hoped that these observations might aid in answering some of the foregoing questions and in determining the functions of the thymus gland and other lymphoid tissue.

As the work progressed the results obtained necessitated the use of a variety of procedures. For this reason, procedure and results are described together.

A method for involuting lymphoid tissue without injuring other tissues was suggested by the work of Bienfait (2) in 1928. He stated that irradiation of the spleen stimulated the production of lymphocytolysin which was distributed in the blood and caused cytolysis of lymphocytes. If it were possible to destroy lymphocytes in lymphoid tissue by irradiating the spleen alone while the rest of the body was protected, the conditions for the above observations would be ideal because the danger of x-ray effects on tissues other than lymphoid tissue would be slight. The following experiment was attempted to test this possibility.

Five 40-day-old rats were anesthetized with ether or sodium barbital and the spleen was drawn through an incision in the abdominal wall and rayed, while the rest of the body was protected completely by a lead shield. The spleen was then replaced in the abdominal cavity and the incision was sutured. From five to seven days later the rats were killed and the thymus glands were examined. The results of the few experiments performed are tabulated in Table I.

These results indicate to us that attempts to produce an appreciable involution of lymphoid tissue by stimulating the spleen to produce lymphocytolysin were not practical. Ferroux, Gayet, and Jolly (4), in 1927, stated that involution of lymphoid tissue by the indirect effect of x-rays does not occur.

It was apparent then that we must resort

TABLE I.—NEGATIVE EFFECTS OF SPLENIC IRRADIATION ON THE THYMUS

Sex	Age (days)	Dose	Body Weight	Days following raying when rat was killed	Thymus Weights Rayed Rats	Normal
M	40	216 r	100 gm.	5 days	0.322 gm.	0.360
F	41	360 r	120 gm.	6 days	0.412 gm.	0.360
F	39	468 r	93.7 gm.	7 days	0.415 gm.	0.360
M	40	1,040 r	.....	6 days	No gross change	0.360
F	40	1,040 r	.....	7 days	No gross change	0.360

In this table "No gross change" indicates that the thymus was not weighed but that it appeared to be of normal size.

to the direct effects of x-rays and irradiate the whole body of the rat if we wished to demolish all of the lymphoid tissue. To test the practicability of this procedure five two-day-old rats were exposed to 280 r and ten to 360 r. Some of these rats were killed a short while after irradiation and others months later. Their thymus glands were examined grossly and microscopically. tissue but not so much as we had hoped to obtain. A more definite involution was caused by 360 r but there resulted, also, a delay in the appearance of hair over the entire body, anemia, stunted growth, and a peculiar nervous complex. This complex was characterized by weakness, partial paralysis, intentional tremor of the extremities, and impaired equilibration. The

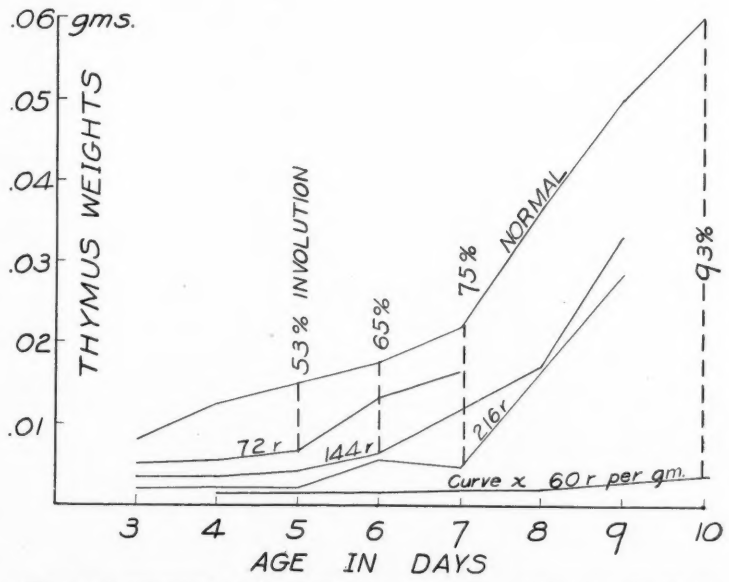

Fig. 1. A comparison of the effects of increasing doses of x-rays on the thymus gland. The vertical interrupted lines mark the maximum extent of separation between the normal curve and the respective abnormal curves. The percentage figures associated with the interrupted lines express the maximum percentage by weight of involution. Sixty r per gram body weight, the dose indicated on the lower curve, is equivalent to a total dose of 360 r. Curve *x* was made by the use of data obtained from an experiment which is described toward the end of the paper.

The results of these examinations were used as an indication of the extent of involution of other lymphoid tissue in the body (Tsuzuki, 10). It was found that 280 r produced some involution of lymphoid smaller dose, 280 r, produced no such complex. When as much as 600 r were administered to rats while their heads were protected by a one-sixteenth inch lead shield, no nervous symptoms developed.

Since 600 r produced no nervous complex when the head was covered, it appeared that the brain was the portion of the body involved in the production of the complex.

We concluded from the results of this group of experiments that a dose of x-rays large enough to produce an appreciable involution of lymphoid tissue inflicted an injury in the brain which produced many nervous symptoms. It then became apparent that the head of the rats must be protected in subsequent attempts to involute lymphoid tissue. Therefore, the plan to destroy all of the lymphoid tissue in the body of the rats (including the head) was abandoned.

We could foresee at this time numerous difficulties if we were to use doses of x-rays larger than 360 r, because this dose had caused the pathology noted above. We decided to analyze the effects of smaller doses of x-rays on the thymus gland in an attempt to establish a method of irradiation that might effectively involute all the lymphoid tissue except that in the head.

To accomplish this purpose different doses of x-rays, 72, 144, and 216 r, were administered to 60 two-day-old rats while their heads were protected by a lead screen. Their body weights were recorded on the day they were irradiated, and on the day they were killed. They were killed on various days from the third to the tenth. Their thymuses were removed, weighed, and examined microscopically. The data obtained for similar days and doses were averaged and plotted as in Figure 1.

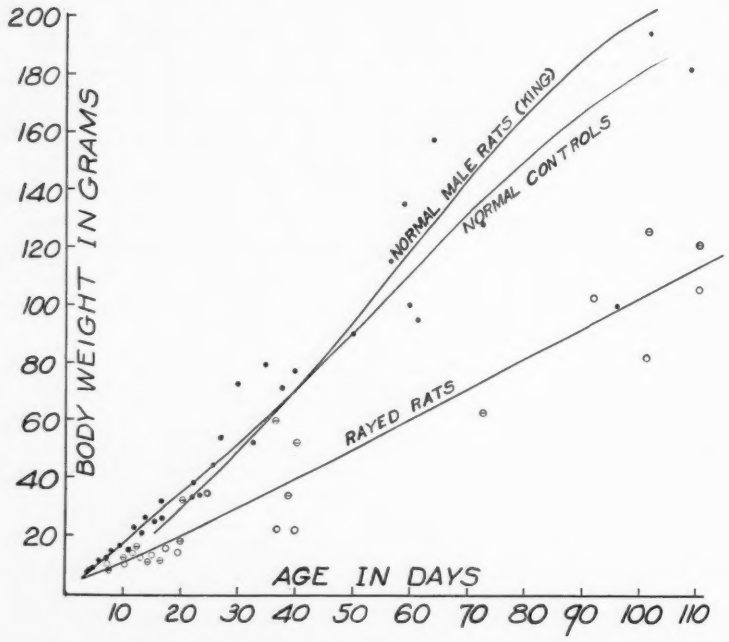

Fig. 2. A comparison of the body growth of normal and irradiated rats. There are two normal curves. The upper one was copied from King (6). The lower one is drawn through the black dots which represent the average weights of litter-mate controls. The average weights of irradiated rats are plotted as follows; males by "⊖" and females by "○."

It can be seen in this figure that a dose of 72 r produced its maximum involution of 53 per cent of thymic lymphoid tissue by weight three days following irradiation. Regeneration began on the same day: 144 r caused 65 per cent involution four days following irradiation. When 216 r were

used a maximum involution of the thymus of 75 per cent occurred by the fifth day following irradiation, and regeneration began on that day. These results indicated that as the dosage of x-ray administered to the rat is increased, the amount of involution of lymphoid tissue is increased and the onset of regeneration is delayed.

Superficial observation of the data accumulated in the above experiment indicated that there was a sex difference in the degree of involution of thymuses. In order to investigate this observation the male and female thymus weights were considered separately. The male thymus weights obtained from rats receiving 72, 144, and 216 r units were averaged separately for the third day. These three averages were then averaged. The same was done for the fourth, fifth, sixth, and seventh days. The data for the females were arranged in the same manner, and all of these averages were tabulated in Table II.

TABLE II.—SEX DIFFERENCE IN INVOLUTION OF THE THYMUS GLAND BY X-RAYS

Age of rats in days	Average weights of thymus glands irradiated with 72, 144, or 216 r		Average body weights of irradiated rats		Weights of control thymus glands	
	Males (gm.)	Females (gm.)	Males (gm.)	Females (gm.)	Males (gm.)	Females (gm.)
3	0.003	0.004	5.9	6.0	0.007	0.009
4	0.003	0.004	7.3	7.2	0.013	0.013
5	0.005	0.006	8.2	7.6	0.014	0.017
6	0.006	0.0068	9.1	7.7	0.015	0.019
7	0.014	0.009	11.2	8.2	0.0195	0.023
9	0.028	0.035	14.2	14.7	0.042	0.041

The results tabulated in Table II indicate that the female thymus is more resistant to x-rays than the male. In the results tabulated for the seventh day, the opposite condition prevails. This can be explained, however, by the fact that the male rats in this case were three grams heavier than the female rats. When a comparison is made of the normal weights of female and male thymuses in the very young rat (Table II), it appears as though the male thymus is lighter than the female thymus. This is probably the reason for the greater weights of the experimental female thymuses above recorded.

At this point in the development of this problem, we perceived by studying our previous results that the percentage of involution of the thymus gland following irradiation with a constant dose of x-rays was inversely proportional to the weight of the gland. Therefore, we decided that more constant results could be obtained if the dose of x-rays was determined by the weight of the gland. This could be done easily because we discovered that the thymus weights in young rats are directly proportional to the body weights of the rats. Consequently, in all of the subsequent experiments the doses of x-rays are expressed as r per gram body weight.

The results compiled in Figure 1 indicate the ease with which the thymus gland can be involuted, and also the difficulty encountered in preventing regeneration of the involuted gland. Regaud and Crémieu (9), in 1912, demonstrated a reduction in the size and weight of thymus glands of young cats that had been exposed to 14 Holzknecht units of x-rays. On the second day this reduction was detectable. On the fifth day the thymus was reduced 80 per cent of its normal weight and at two weeks 90 per cent of the thymus had degenerated. They also noted that regeneration began on the fifteenth day from lymphocytes which had remained unaffected. We anticipated destruction of the regenerative power of the thymus gland if a second dose of x-rays were given preceding that time when regeneration might begin. Microscopic examinations of the involuted thymus revealed only a few lymphocytes at this time. We hoped that these cells might be killed by a second dose of x-rays and the source of regeneration eliminated.

The following experiment was designed in accordance with these ideas. A dose of 40 or 45 r per gram body weight was given to 24 two-day-old rats while their heads were protected by a lead plate. The same dose was repeated on the fifth day under the same conditions. All of the above animals were controlled by litter-mates. Some of the animals were killed during the first few weeks of the experiment. The

thymuses were removed, weighed, and examined microscopically. Those animals which were not killed early in the experiment were weighed frequently; thus a record of their growth was obtained.

The results of this experiment concerning the thymus gland and lymphoid tissue were discarded because marked delay in growth of the animals resulted. Incomplete involution of the thymus glands was revealed by gross examination. The data demonstrating stunted growth of the animals are presented in Figure 2. Photographs of two irradiated rats and two normal rats are presented in Figure 3 for comparison.

Fig. 3. The two upper rats had the whole body irradiated except the head. The two lower rats are 20-day-old litter-mate controls.

To eliminate the possibility that the stunted growth occurred because of the effects of involution of lymphoid tissue and was not the direct effect of the x-rays, 10 rats were irradiated in the same fashion as those above except that the lead shield covered the cranial part of the body as far down as the xiphoid process of the sternum. In these animals that portion of the body which was exposed to x-rays was definitely stunted in growth, as illustrated in Figure 4. It appeared from these experiments that the retarded growth produced in these rats was a direct effect of the x-rays. Brooks and Hillstrom (3), in 1933, investigated the effects of x-rays on bone growth, and they compiled a large bibliography which dated back to the original work of Perthes in 1903.

The results obtained thus far indicated to us that attempts to produce a generalized involution of lymphoid tissue without injuring other tissues were futile. The fact that a dose of x-rays large enough to produce an appreciable involution of lymphoid tissue inflicted an injury in the brain and stunted growth indicated to us that in all of the remaining experiments the body of the rats must be protected by a lead shield while the x-rays were administered through an aperture over the thymic area.

In the first group of experiments after this new routine was established, an attempt was made to repeat approximately the conditions of the previous experiment in which stunted growth resulted, so that

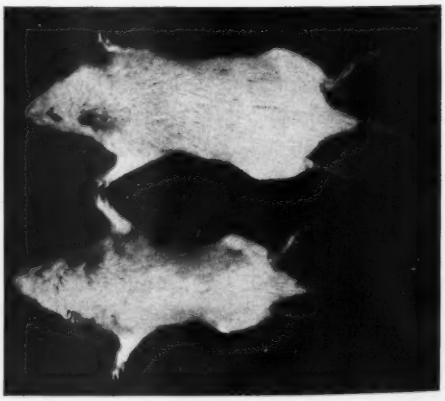

Fig. 4. The caudal one-half of the lower rat was irradiated. The upper rat is a 35-day-old litter-mate control.

the effects of involution of the thymus gland on body growth could be compared with the results of the previous experiment.

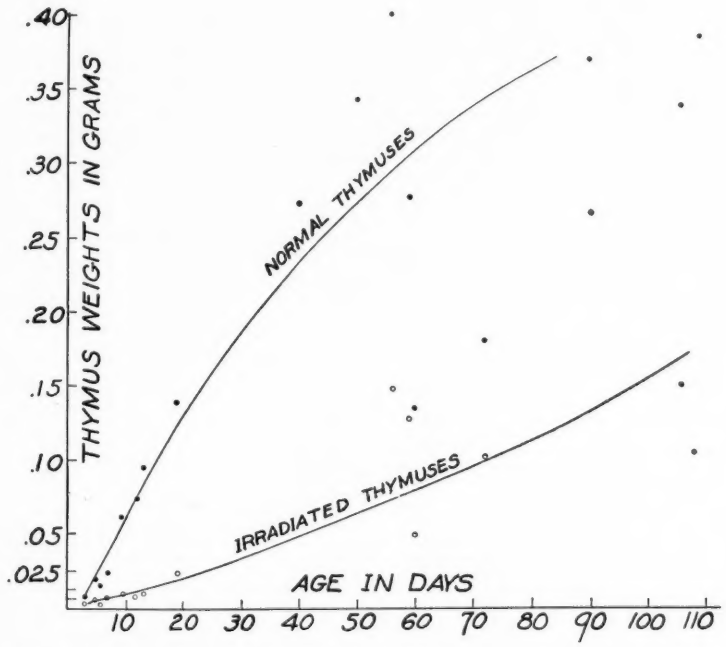

Fig. 5. A comparison of the weights of normal thymuses and thymuses irradiated with two doses of 45 or 50 r per gram body weight. The circles represent the average thymus weights of irradiated rats. The black dots denote the litter-mate controls.

Forty rats were irradiated with 45 or 50 r per gram body weight on the second day of life. The same dose was repeated after three days. Litter-mate controls were kept. The rats were killed at various ages ranging from three to 110 days and the thymuses were removed and weighed. The resulting data for similar days were averaged and plotted in Figure 5. Accurate data on the growth of these animals were kept and plotted in Figure 6.

In Figure 5 it can be seen that the irradiated thymuses were partially involuted and remained so until the rats were 110 days old. Complete involution was not obtained. Figure 6 indicates that there was no effect on the body growth of rats when their thymuses were involuted to the extent shown in Figure 5. This result is in accordance with the work of Park and McClure (8), who demonstrated that thymectomy caused no alteration in growth. A comparison of the growth curve obtained in this experiment with that resulting in the previous experiment reveals quite a contrast.

Because of the fact that the doses of x-rays given thus far had not produced a lasting involution of the thymus, a series of experiments was performed in which one large dose of x-rays was administered in an attempt to produce a permanent involution of the thymus. In view of the fact that complete thymectomy is not followed by regeneration of the thymus, and since Regaud and Crémieu (9) state that complete destruction of the thymus of the kitten was caused by the administration of 50 Holzknecht units of x-ray, it seemed logical to think that a dose of x-rays which

would produce a complete involution would prevent regeneration of the thymus.

One dose of 60 r per gram body weight was administered to 12 two-day-old rats. They were killed on various days following irradiation and their thymuses were removed and weighed. During the eight days following irradiation involution of the thymus gland occurred to the extent of 93 per cent by weight. Even after this amount of involution, regeneration occurred. The data from this experiment were plotted in Figure 1, because they supported the conclusion that as the dose of x-rays administered to the thymus glands is increased, the percentage of involution is increased and the onset of regeneration is delayed. The curve which was made from the data of this experiment is indicated in Figure 1, by the letter *x*.

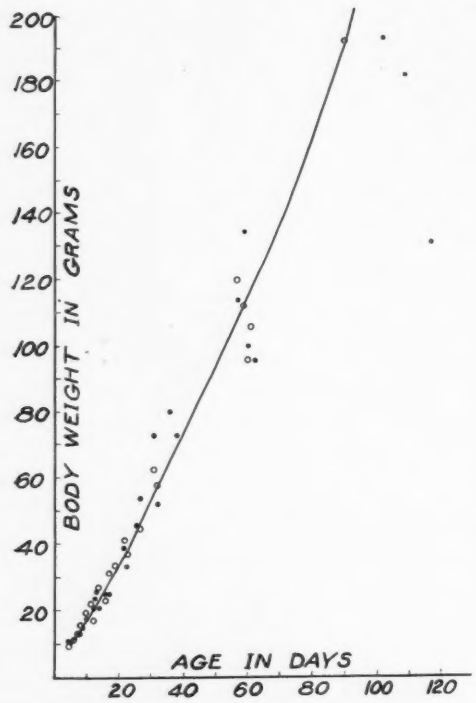

Fig. 6. A comparison of the body growth of normal rats and rats following involution of the thymus gland to the extent indicated in Figure 5. The circles indicate the average weights of the irradiated animals. The black dots represent the average weights of normal control animals.

At this time we made an inventory of all of the x-ray doses, to date, in terms of r per gram body weight. We found that single doses of 10, 20, 35, 45, and 60 r per gram body weight and double doses totalling 80, 90, and 100 r per gram body weight had been given.

We decided, therefore, to determine the effects of doses of x-rays larger than 100 r per gram body weight. When doses of 108, 126, 128, 144, 160, and 216 r per gram body weight were administered to two-day-old rats a severe x-ray burn resulted seven days following irradiation. In association with the burn a marked paralysis of the forelimbs occurred. All of the rats died before they were four weeks old, in most instances, death occurring on the thirteenth postnatal day. The parents devoured all of the irradiated rats except eight which we retrieved from the cages. When the markedly atrophied thymus glands from these rats were examined histologically, we found lymphoid tissue in three. In the other five, no lymphoid tissue was demonstrable. Numerous mast cells were seen in all of the glands.

We concluded from this experiment that a dose of x-rays large enough to produce complete involution of the thymus gland in very young rats caused death to the animals because of marked damage to other tissue.

CONCLUSIONS

1. Gross involution of the thymus gland by the indirect effects of x-ray irradiation of the spleen does not occur.

2. Irradiation of the whole body of two-day-old rats with 360 r produces a nervous complex which is characterized by an intention tremor and a loss of equilibration. The site of the lesion is probably in the brain of the rat.

3. As the dosages of x-rays administered to the thymus glands of two-day-old rats is increased, the percentage of involution is increased and the onset of regeneration is delayed.

4. Growth may be retarded by x-rays. This retardation is a direct effect of the x-rays and appears to have no relation to lymphoid tissue.

5. Partial involution of the thymus gland of rats by x-rays does not affect the growth of the rat.

6. The dosage of x-rays required to produce a complete and permanent involution of the lymphoid tissues of the body is so great that it causes other deleterious effects.

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THE MEASUREMENT OF TISSUE DOSE IN TERMS OF THE SAME UNIT FOR ALL IONIZING RADIATIONS

By G. FAILLA, D.Sc., Memorial Hospital, *New York City*

IN radiation therapy it would be obviously of great advantage to choose a unit of dose such that the same biological effect would be produced by a given dose, irrespective of the quality, or even kind, of radiation employed, provided, of course, that all other conditions remained the same. There is enough experimental evidence available to-day to prove that this ideal situation cannot be realized by the adoption of any one unit of dose, in the quality range which includes both ordinary x-rays and gamma rays. It becomes necessary, therefore, to examine the problem with the object of selecting a unit which approaches the ideal one as closely as our present knowledge permits.

Taking for granted the existence of a difference in biological effect produced by radiation of different wave length (irrespective of the unit of dosage) the quasi-ideal unit would be one which makes possible the specification of equivalent biological effect by the smallest number of dosage factors. The smallest possible number in which such a "biological dose" may be expressed, is two: one representing the *quantity factor* of the dose, and the other the *quality factor*, both referring to the point at which the biological effect is produced. By these two factors one must be able to express doses of (ionizing) radiation of any wave length, which are biologically equivalent, when all other conditions are identical. Biological equivalence in this connection must necessarily mean equivalence in the *degree* of effect produced. If the *kind* of effect is different, no comparison at all is possible. In the ordinary therapeutic range of wave lengths, it may be assumed that there is an equivalence in kind. That is, erythema, tumor regression, and a host of other biological effects, are all produced by radiation of widely different wave lengths, irrespective of any possible differences in the mechanism by which these biological changes are brought about.

The biological dose, D_b, may be expressed as follows:

$$D_b = D\ q\ b,$$

where D = Dose, or quantity factor, which can be measured and expressed in suitable units.

q = Quality factor, representing the biological effectiveness of radiation with respect to wave length.

b is a factor depending on all other conditions—largely biological—which are assumed to remain constant, when the influence of wave length is being investigated. (Therefore it can be taken as unity in the present case.)

We shall now inquire how the dose D should be measured and in what unit it should be expressed in order that the quality factor q shall depend only on the wave length of the radiation, as it should when all other conditions are constant. It has been stated many times, and it is obvious, that the part of the radiation which is responsible for the biological effect is that which is "absorbed" by the living organism. In the case of ionizing radiation, not all the absorbed energy manifests itself in the form of ionization, but the ratio between the total absorbed energy and that which is utilized in forming ions is, so far as we know, substantially independent of the wave length, in the present therapeutic range. Thus, since the two are related by a proportionality factor, one may take ionization as a measure of energy absorbed. This refers, of course, to the ionization produced in the living material, at the point where the biological change takes place. Since the number of electrolytic ions pres-

ent in the material is very much larger than the number of radio-ions which may be set free by a therapeutic dose of radiation, it is practically impossible to measure directly the radiation ionization. This difficulty may be overcome provided we can measure something which is related by a simple proportionality factor to tissue ionization at the point in question. Since ionization in gases may be measured very readily, it would be very convenient to take advantage of this. We shall inquire, therefore, under what conditions the ionization in a gas may be expected to be proportional to that in living tissue.

The interaction of radiation and matter depends on the number of electrons in the material, and on the atomic numbers of its constituent chemical elements. Therefore, the energy absorbed from a beam of radiation per gram of tissue is the same as that which would be absorbed per gram of a gas containing the same chemical elements in the same proportions, under comparable conditions. The number of ions would not be the same, since it depends also on the chemical state of the matter, but the proportionality factor would remain constant throughout the wave length range used in therapy. There are two different mechanisms by which radiation transfers energy to matter, although in both cases the transfer occurs by setting electrons in motion. In the photoelectric process, the controlling factor is the atomic number of each chemical element in the material, whereas in the Compton process the controlling factor is the total number of electrons present. Whether one or the other predominates, depends on the wave length of the radiation. For x-rays produced at voltages higher than 150 or 200 kv., and matter composed of low atomic number elements (such as living tissue) photoelectric absorption is negligible. Accordingly in this case the proportionality between ionization in tissues and in a gas may be expressed with sufficient constancy with respect to wave length for practical purposes, even when the chemical composition of the gas is not exactly the same as that of the tissue in which the biological effect is produced. Air, being composed largely of nitrogen and oxygen, is probably a satisfactory gas to use in this range of wave lengths.

In recapitulation, we may say that in the wave length range of filtered 150 to 200 kv. x-rays and gamma rays, we may expect reasonably constant proportionality factors between: (1) ionization in air and ionization in tissues, (2) ionization and energy absorbed in tissues, and consequently (3) ionization in air and energy absorbed in tissues, provided the ionization in air is produced under conditions comparable to those obtaining in the irradiated tissue. Hence, since absorbed energy must be considered as the ultimate cause of the biological change, air ionization will bear the same relation thereto. Thus the simplest correlation between cause and effect may well be expected by using air ionization (under suitable conditions) to represent the cause, namely the dose of radiation. In the case of soft x-rays, air is not a suitable gas because of the difference in atomic numbers of its constituents (nitrogen 79 per cent, oxygen 21 per cent) and those of tissue (roughly oxygen 65 per cent, carbon 18 per cent, hydrogen 10 per cent, nitrogen 3 per cent). Furthermore, the influence of the small proportions of elements of higher atomic number, (calcium, phosphorus, potassium, sodium, etc.) present in tissues but absent in air, is probably considerable in the range of soft x-rays.[1]

The requirement that the ionization in the gas (air), which is to be taken as a measure of dose, must be produced under the same conditions as those obtaining in the living material during the irradiation, at the point where the biological effect is produced, has been emphasized already. It is the main purpose of this paper to describe methods and means by which this requirement may be met satisfactorily in all cases of practical importance, insofar as our present knowledge permits.

[1] This problem is being investigated experimentally in our laboratory by Dr. R. Naidu, of the Tata Memorial Hospital, Bombay, India.

A knowledge of the "skin dose" in radiation therapy is of paramount importance, since, in general, it is skin damage which limits the amount of radiation that may be delivered to a deep-seated tumor. Where the seat of the skin injury is, or what particular layer of the skin is most vulnerable, is of no concern in the present discussion. It is obvious, however, that in order to study the reaction of the skin to radiation, it is essential to know the energy absorbed by different layers of the skin, and, perhaps, the subcutaneous tissues. In the range of ordinary x-rays and gamma rays we may take ionization in air as a measure of energy absorbed in an equal mass of tissue. How shall we determine the air ionization at different levels in the skin, including the surface? It is evident *a priori* that the desired information cannot be obtained directly by the use of the well-known thimble chamber, for such a chamber is necessarily too large in comparison to the thickness of human skin. Both the air space and the solid walls of the chamber disturb the physical conditions which influence the ionization at the surface of the skin, even when the chamber is of the so-called air wall type. Two absurd requirements should be met by an ionization chamber suitable for this purpose: (1) it should have no walls, and (2) it should have no air volume. Surprising as it may seem to the uninitiated, these conditions can actually be fulfilled in practice. The general method is as follows: For the surface dose we wish to determine the ionization in a vanishingly thin layer of air in actual contact with the skin, in order that the back-scattered radiation may be properly evaluated. There must not be anything in the path of the incoming radiation which is not present during the treatment. Let us take a hypothetical ionization chamber with two walls, each one square centimeter in area, separated by an air space one millimeter thick. We place the chamber on the surface of the skin at the point where the ionization is to be determined and we take a reading. We then decrease the thickness of the chamber walls by some means or other and take another reading under the same conditions. We repeat the process until the walls are as thin as they can be made. From these readings we obtain a curve which shows the variation of the ionization in the chamber with wall thickness. The curve is then prolonged—extrapolated—to zero wall thickness and the value of the ionization which would be obtained in the same chamber with vanishingly thin walls, can be read on the ionization reading scale.

We have assumed the thickness of the air layer in the hypothetical chamber to be one millimeter. In order to reduce this to the vanishing point, we may make use of an extrapolation method similar to the one just described. Maintaining the wall thickness constant and at its lowest practical value, readings are taken with air layers of different thicknesses, down to a minimum which is set by instrumental limitations. It is evident that the larger the air thickness the larger the ionization reading, and that when the air thickness is zero, the reading must also be zero. On the other hand, the ionization per unit volume of air has a definite value even when the air space is vanishingly small. From the actual ionization readings we derive the values of the ionization per cubic centimeter of air. Plotting these, we obtain the relation between air layer thickness and ionization per cubic centimeter. Extrapolating the curve to zero air thickness, one obtains the ionization per cubic centimeter which would be produced in a chamber having very thin walls and a vanishingly small air thickness, placed at the surface of the skin. By means of the wall thickness curve previously obtained, one can correct this value for the thickness of the chamber wall, and the result will represent the ionization per cubic centimeter of air at the very surface of the skin, under the conditions in which the skin is irradiated.

Nothing has been said about the nature of the chamber walls, and it may be assumed that, since the influence of the wall thickness is eliminated by extrapolation, the material of which it is made plays no

part in the final results. However, the ionization produced in the thin air layer is due almost entirely to electrons which

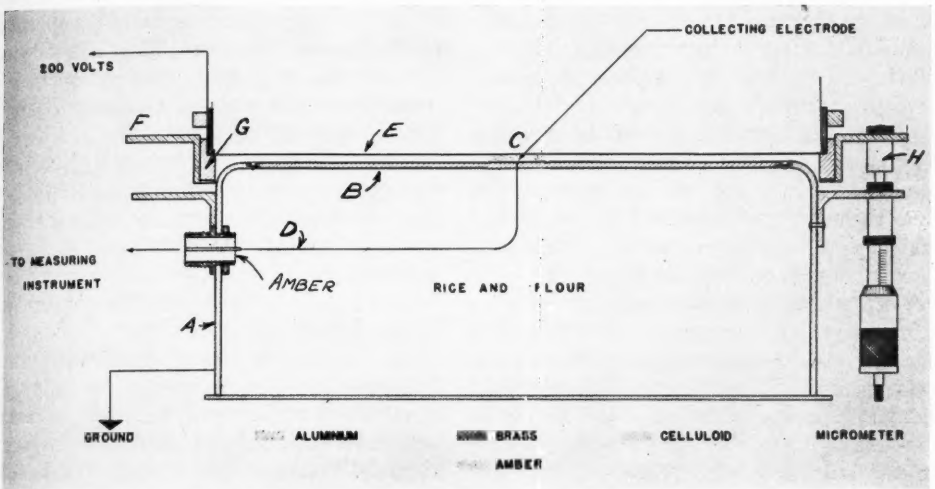

Fig. 1. Extrapolation ionization chamber for the measurement of tissue doses in roentgen and telecurie therapy.

either originate in the walls or reach the air volume by penetrating through them. Hence the experimental readings are influenced markedly by the material of which the chamber is made. The reasons for the use of air equivalent materials in the construction of thimble chambers are well known. They apply equally to the present case. In general it is even better to have tissue equivalent materials.[2] The hypothetical ionization chamber considered so far is not practical. The construction of a suitable one involves many difficulties and much time was spent by us before a satisfactory solution was obtained. The one which has been used in our laboratory during the past year is shown in Figure 1. An aluminium pot, A, about 30 cm. in diameter and 15 cm. deep, was used as the foundation. The bottom of the pot was turned out and a celluloid disk, B, 3 mm. thick, was screwed on in its place. The top of the celluloid disk was coated with India ink, and by means of a sharp compass a circle 2.96 cm. in diameter was scribed at the center. The inked surface within the circle constitutes the collecting electrode, while the outer surface which is conductively connected to the aluminium pot, serves the purpose of a guard ring and helps provide a uniform electrostatic field over the entire area of the collecting electrode. When a null method of measurement is used, a very narrow and superficial scratch made with the compass is sufficient to provide good insulation between the collecting electrode and the adjoining conducting surface. Thus very little field distortion occurs at the boundary of the collecting electrode, and its effective area may be calculated from the diameter of the circle passing through the center of the insulating gap. The collecting electrode is connected to the current measuring instrument through a very fine rubber insulated wire D.[3] The wire does not extend

[2] This is imperative when the ionization to be measured is produced by the passage of neutrons through tissue.

[3] This connection gave us considerable trouble, and several schemes were tried. The details of the one used finally have been forgotten. It may be useful to mention that at first we tried to make the connection between the collecting electrode and the amber bushing by running a fine aluminium wire in a slot in the celluloid disk. The slot was filled with paraffin. For some unaccountable reason—which we did not spend time to investigate—this collecting electrode system acted as if it were the pole of a battery, and supplied current

to the surface of the collecting electrode, but good electrical contact is effected by carbon. The lower side of the celluloid disk, *B*, was also coated with ink, except for a small space around the wire connection. The space below the electrode was filled with rice and flour to provide a convenient substitute for tissue.

The upper electrode was made in such a way that it could be changed readily without disturbing the set-up appreciably. The thinnest one consisted of ink-soaked silk chiffon, stretched over an aluminium hoop about 30 cm. in diameter. The mass per square centimeter of this material is 2.0 mg., which corresponds to a thickness of 0.02 mm., assuming a density of one gram per cubic centimeter. Similar but thicker upper electrodes were made of parchment, and of "Masonite pressdwood," the latter being used for thicknesses greater than three millimeters. This material is readily obtainable at low cost in sheets of two or three different thicknesses. It consists largely of wood pulp, has a density of 1.01 gram per c.c. and an ash residue of 1.67 mg. per c.c., not unlike that of soft tissues.

In order to provide simple and precise adjustment of the spacing between electrodes, three micrometer screws were mounted as the one shown in the figure. The lower aluminium ring on which the micrometers are rigidly mounted, was fitted to the aluminium pot and its surfaces were machined at the same time that the recess for the celluloid disk was turned out in the lathe, thus insuring parallelism between the two. The aluminium ring, *F*, was machined a second time after the celluloid ring, *G*, had been fastened to it, to make sure that the plane of the recess into which fits the upper electrode was parallel to the plane of the ring. The celluloid ring serves to insulate the charged upper electrode from the earthed aluminium parts. Three carefully adjusted steel anvils, *H*, rigidly fastened to the ring, *F*, register with the appropriate micrometers, so that when their readings are the same, the two electrodes are parallel to each other.[4] Proper registration of anvils and micrometer screws is maintained by three guides not shown in the figure.

A null method of measuring the ionization current is always used. The collecting electrode is maintained at earth potential, which is also the potential of the guard ring. Thus there is no leakage to take into account, and the electrostatic field between the electrodes is perpendicular thereto and uniform. In this way the air volume in which the ionization is measured is determined by the area of the collecting electrode and the distance between electrodes. With the silk chiffon electrode in place, practically all the incoming radiation and its secondary electrons can reach the air volume. The influence of even this thin layer of matter can be eliminated by extrapolation, as already described. When the spacing is very small and the beam larger than the collecting electrode (which, of course, should always be the case) the air volume receives the appropriate quota of the back-scattered radiation. However, there are certain things which should be examined critically. Is the back-scattered radiation in this chamber, with its 3 mm. celluloid electrode and the rice and flour backing, the same as it would be from a mass of tissue of equal mass and shape? This depends on the type and quality of the radiation considered. For ordinary x-rays

of relatively large magnitude to the measuring instrument for long periods of time. The paraffin by itself could not have been responsible for the effect, since in another chamber of this type in which the wire was embedded in a block of paraffin, used for months before the present chamber was constructed, no such effect was present at any time. Recently, through the courtesy of the Plastics Department of E. I. du Pont de Nemours and Company, we have obtained an electrode in which a very fine piano wire is embedded between two thin sheets of "Lucite" composited into one solid sheet under high pressure and appropriate temperature. A similar electrode made of "Styrol" is also available. Lack of time has prevented a study of these electrodes.

[4] We have found in actual use that the celluloid disk does not remain plane and it is very difficult to determine the absolute spacing with great precision. The relative spacing can be determined very accurately from the micrometer readings, and this is sufficient for most practical purposes.

and gamma rays the difference is negligible within the limits of experimental error in biological investigations. We have thought that the difference in chemical composition and density between celluloid and tissue may cause a slight error. Inasmuch as the contribution to the measured ionization of the back-scattered radiation is due almost entirely to secondary electrons which leave the surface of the lower electrode, we have thought that the ink coating (carbon) may provide a lower quota than the skin would when the radiation is very soft. These points, which are probably of little importance in the present practical range of therapeutic radiation, are being investigated. It is hardly necessary to point out that the shape and size of the scattering material (rice and flour in this case) should be the same as the part of the body for which the skin dose is desired. The present chamber was constructed primarily for the purpose of comparing surface and depth doses measured under the same conditions by this method and by the usual thimble chamber method. Chambers of more general applicability are in the course of construction.

We have indicated how the ionization in air at the very surface of the skin can be determined. The ionization in a vanishingly thin layer of air at any skin or tissue depth can be determined in an analogous way, except that in this case only extrapolation to zero air thickness is necessary. By using for the upper electrode sheets of parchment or other suitable material, of appropriate density and thickness, it is a simple matter to determine the air ionization which corresponds to different depths in the skin and subcutaneous tissues.

A great deal of work has been done with chambers of this type in our laboratory by Mrs. Edith H. Quimby, Mr. L. D. Marinelli, and others, who will publish the results in the near future. At this time we shall discuss only the correlation of ionization measured by this method and skin erythema, in order to bring out an important point in the problem of choosing a unit of dose. Measurement of the air ionization at the surface and at different depths have been made with this chamber under comparable conditions, using three widely different qualities of radiation: (1) soft x-rays, produced at 85 kv., filtered by 1 mm. of aluminium, having a half value layer of 1.7 mm. of aluminium; (2) hard x-rays, produced at 200 kv., filtered by 0.5 mm. of copper and 2.5 mm. of aluminium, having a half value layer of 1 mm. of copper; (3) gamma rays from a four-gram radium bomb with an estimated metallic filter equivalent to 2 mm. of lead, and a secondary filter of 3 mm. of celluloid (which in the erythema tests was in contact with the skin). Previous experiments had shown that in the case of x-rays, extrapolation to zero thickness of upper electrode was unnecessary. Accordingly, only the 0.18 mm. parchment electrode was used. In the case of gamma rays, the upper electrode was a sheet of celluloid 3 mm. thick, corresponding to the celluloid filter used in contact with the skin in the erythema determinations. Extrapolation to zero air thickness was carried out in all three cases. The only appreciable difference in the conditions under which the ionization measurements and the erythema tests, respectively, were carried out, resides in the much larger volume of scattering material (rice and flour) in the chamber as compared to the human forearm. However in all cases the measurements were made with radiation fields of the same (small) size as used in the erythema tests. The possible error caused by this difference does not alter the general conclusions, and may be ignored for the present. The ionization doses of the three qualities of radiation required to produce the threshold erythema[5] on the forearm of the average white adult are: 0.36×10^{15}, 1.05×10^{15}, and 1.75×10^{15} ion pairs per gram of air, respectively, for soft x-rays, hard x-rays, and gamma rays. These figures refer to the ionization produced at the very surface of the skin. It is important to note that the relative values remain essentially the same no matter what depth within the skin is chosen for the seat of the

[5] When the radiation is administered continuously during a period not exceeding about two hours.

biological reaction. If it is assumed that the threshold erythema is one manifestation of the changes which take place in all underlying tissues, the difference between the ionization doses for 85 kv. and 200 kv. x-rays, will be still greater, since under the conditions of the experiments the decrease in radiation intensity with depth was greater in the case of the softer x-rays. Assuming that the dose is properly measured by the method described here, it is evident that the same dose of radiation does not produce the same biological effect (threshold erythema) when the quality of radiation is different. Except for minor refinements we can find nothing which might vitiate the general results.

The main point we wish to bring out in this connection is not the wave length dependence of skin erythema, but the simplification which may be brought about by the choice of a suitable unit of dosage. If we agree by definition that the biological dose of radiation is the same irrespective of quality, provided all other conditions remain constant, we have for the threshold skin erythema:

$$0.36 \times 10^{15} \times q_{85} = 1.05 \times 10^{15} \times q_{200} = 1.75 \times 10^{15} \times q_r.$$

Thus the relative values of the quality factor q in this case are:

For 85 kv. x-rays, H.V.L. 1.7 mm. Al, $q_{85} = 2.9$

For 200 kv. x-rays, H.V.L. 1 mm. Cu, $q_{200} = 1$

For filtered gamma rays $q_r = 0.6$

assigning the value 1 to the quality factor for 200 kv. x-rays. This means that a dose of 85 kv. x-rays, of 1.7 mm. Al H.V.L., 4.8 times *smaller* than the dose of gamma rays is necessary to produce the threshold erythema.[6] Similarly, in the case of 200 kv. x-rays of 1 mm. Cu H.V.L., the threshold erythema dose is 1.7 times smaller than for gamma rays. The quality factor, therefore, furnishes an index of the biological effectiveness of radiation of different wave lengths for a particular effect produced under comparable conditions. A knowledge of this factor is essential for proper dosage in radiation therapy, but unfortunately the relative numerical values of the factor can be obtained only through extensive experimentation (both physical and biological).

Ionization doses in the illustrative case just discussed were expressed in terms of the number of ion pairs produced per gram of air. It is important to consider now how measurements made in roentgens can be utilized for this purpose. The method of measuring skin dose, which we have described, can hardly be contested, although there may be some differences of opinion concerning details of the apparatus or the depth in the skin at which the measurements should be made. Therefore, it is reasonable to assume that skin doses measured in this way are very nearly correct, the criterion of correctness being the measurement of something which is related to the immediate cause of the biological effect (*i.e.*, energy absorbed by the tissue) by a constant proportionality factor. In practice, an x-ray machine in the radiological clinic is calibrated by means of a suitable thimble chamber, and the radiation output at a certain point in the beam, under given conditions, is expressed in roentgens per minute. The radiologist then places a patient with a part of his skin at the same point in the radiation beam. What is the skin dose delivered in a certain treatment, and in what unit can it be expressed? The usual procedure[7] is to multiply by the appropriate backscatter factor and the time in minutes the r per minute value obtained from the measurement with the thimble chamber suspended in air, and to call the product the number of roentgens which the skin receives, that is, the skin dose. In so doing, the radiologist uses the roentgen for the

[6] It should not be assumed that the ratio is the same for all biological effects. It is definitely known that this is not the case. (*Cf.* Failla and Marinelli's paper on gamma-ray measurements in the August, 1937, number of the "American Journal of Roentgenology and Radium Therapy.")

[7] Some prefer to make the thimble chamber measurement on the skin of the patient. This is immaterial.

purpose for which it was originally intended, although strictly speaking, the wording of the definition of the unit does not justify this use. For the moment we need not insist on this point. The obvious fact is that the skin dose must include the contribution due to the back-scattered radiation. Since no unit of "tissue dose" has been adopted, the roentgen is generally used for this purpose as well, explicitly or implicitly. Following the usual procedure, therefore, we shall determine the surface doses for the three qualities of radiation, by means of suitable thimble chambers "half submerged" in the tissue substitute (water or pressdwood).

It so happens that in the quality range of ordinary x-rays, measurements of *surface dose* with the thimble chamber we used are in reasonably good agreement with the corresponding extrapolation chamber measurements. In the case of gamma rays, however, there is a large discrepancy. The details of the measurements are as follows: In order to make sure that the gamma rays reaching the skin in the erythema tests did not contain spurious secondary electrons, a sheet of celluloid 3 mm. thick was placed on top of the skin, and the four-gram radium pack was brought in contact with the celluloid also. Under these conditions the skin was at a distance of 6.3 cm. from the radium. The extrapolation chamber measurements were made with an upper electrode of the same material and thickness (3 mm. celluloid), the only difference being that in this case the celluloid was coated with ink. Readings were taken with different electrode spacings and by extrapolation was obtained the value of the ionization per cubic centimeter in a vanishingly thin air space between the celluloid electrodes at the 6.3 cm. distance. The measurements with the thimble chamber could not be made at the same distance, since the celluloid secondary filter was in the way. Readings were taken, however, with the chamber touching the celluloid sheet and at greater distances. From the curve thus obtained, the reading at 6.3 cm. distance was determined with considerable precision. We have made similar measurements on numerous occasions, with and without back-scatter. With the chamber half submerged in a tank of water, the back-scatter amounts to 11 per cent. The thimble chamber is spherical, with an inside diameter of 1.52 cm., and a celluloid wall 1.4 mm. thick. The stem through which connection to the measuring instrument is made, is about 7 mm. in diameter. Objections may be raised to the use of this chamber for gamma-ray measurements on the ground of insufficient wall thickness. We know, however, that a thicker wall would not alter the result appreciably in this case.[8] Accordingly, we may take for granted that the measurements with the thimble chamber were made under conditions which are very nearly those recommended by several investigators for the measurement of gamma rays *in roentgens*. The effective radiation intensity at the 6.3 cm. distance determined in this manner by the thimble chamber was found to be 12.3 r per minute, including the back-scattered radiation from a large tank of water. On the other hand, the corresponding value obtained with the extrapolation chamber was 9 e.s.u. per c.c. per min. If the conditions under which the ionization was produced in the air volume of the extrapolation chamber meet the requirements set forth by the proponents of the thimble chamber method for measuring gamma rays in roentgens, 9 e.s.u. per c.c. per min. are equivalent to 9 r per min. Since the two methods of measurement give values of presumably the same quantity, which differ considerably, one or the other or both methods must be incorrect.

L. H. Gray's work (1, 2) has been quoted repeatedly in support of the thesis that a small thimble chamber with "air walls" three or four millimeters thick measures gamma rays in roentgens. We see no reason why this should not be so, but at the the same time we see no reason why the con-

[8] At any rate, those who might raise the objection would expect the reading with this chamber to be too low. As a matter of fact it is already much higher than that obtained with the extrapolation chamber (*infra*).

ditions obtaining in the air volume of the extrapolation chamber do not meet the requirements set forth by Gray. Mayneord (3) in his recent precision measurements of gamma rays used a cylindrical thimble chamber 2 cm. in diameter and 2 cm. long (inside dimensions). The diameter of the collecting electrode in the extrapolation chamber, 2.96 cm., is not much larger. Therefore the maximum linear dimension of the "air cavity" in our case cannot be said to be too large. The other dimension (height of cylinder) was always much smaller than in Mayneord's case, 0.5 to several millimeters. The air volume in the extrapolation chamber is at the center and between two disks of celluloid 30 cm. in diameter and 3 mm. thick. When the spacing is 0.5 mm., is it not reasonable to assume that the ionization is measured in an air cavity effectively surrounded by celluloid? Furthermore, by extrapolation we should obtain the value of the ionization per c.c. with the celluloid plates (almost) in contact, in which case it would be hypercritical to say that the air volume was not completely surrounded by celluloid. We do not wish to take a definite stand on this matter at this time, but it is obvious that further investigation of the problem in different laboratories is highly desirable before a generally acceptable conclusion may be reached. However, the following considerations may provide a clue.

The ionization produced in a thick-walled thimble chamber is almost entirely due to electrons originating in the walls. The latter may be divided into: (1) front wall, (2) side walls, and (3) back wall. The contribution of each may be ascertained by suitable experiments. It is found then that quite a high percentage of the ionization is due to the presence of thick side walls. In view of the fact that the ejection of recoil electrons is predominantly in the forward direction, it would appear that better relative utilization of those originating in the side walls will result when the latter are long. Most of the experimenters who have worked on the problem of measuring gamma rays in roentgens have used thimble chambers in which the three linear dimensions have not differed greatly. Accordingly the contribution of the side walls has been considerable. In the case of the extrapolation chamber, the height of the cylindrical air volume is very small in comparison to the diameter, and besides there is no side wall. Nevertheless, as already pointed out, when the air layer is vanishingly thin, the volume in which the ionization is measured may well be considered to be completely surrounded by celluloid. The problem then resolves itself as to whether the presence of thick side walls in the ordinary thimble chamber causes an excessive contribution of electrons to the enclosed air volume. This point deserves careful study.

Returning to the problem of expressing the biological dose for the threshold erythema reaction produced by the three qualities of radiation, in terms of thimble chamber measurements in all three cases, we find:

$$D_b = D\,q = 225 \times q_{85} = 650 \times q_{200} = 1490 \times q$$

in which D is expressed in roentgens, with approximate allowance for backscatter. Whence, taking $q_{200} = 1$, as before, the relative values of q are:

For 85 kv. x-rays, H.V.L. 1.7 mm. Al, $q_{85} = 2.90$,

For 200 kv. x-rays, H.V.L. 1 mm. Cu, $q_{200} = 1$,

For filtered gamma rays, $q = 0.44$.

Since q represents the biological effectiveness of radiation with respect to quality, it is evident that the threshold erythema is not independent of wave length. This conclusion is in accord with the one arrived at previously in the case of measurements of the ionization dose by means of the extrapolation chamber. That the same general conclusion should be reached is obvious when one considers that the relative biological effectiveness of radiation of different wave lengths is dependent on biological factors which play no part in the measurement of the dose by physical means. The values of q for soft and hard

x-rays are the same as before, because measurements of surface dose by the extrapolation and thimble chamber methods are in good agreement in this quality range. The values for gamma rays are quite different, which means that both cannot be correct. If the extrapolation chamber measures the surface ionization dose of rays correctly, it is necessary to reduce the reading obtained with the thimble chamber to that of the extrapolation chamber, in order to make the proper correlation between dose and biological effect. This can be done by introducing a correction factor f which can be determined by experiment. In the case under consideration the surface dose of gamma rays required to produce the threshold erythema is 1,490 r, assuming that the thimble chamber measures gamma rays in roentgens, and that it is proper to use this unit in cases where the back-scattered radiation is included. This is equivalent to $1{,}490 \times 1.62 \times 10^{12} = 2.41 \times 10^{15}$ ion pairs per gram of air. The corresponding quantity obtained with the extrapolation chamber is 1.75×10^{15} ion pairs per gram, and therefore the correction factor is

$$f = \frac{1.75 \times 10^{15}}{2.14 \times 10^{15}} = 0.73.$$

Hence, if the surface dose of gamma rays is measured in roentgens by a thimble chamber, we have

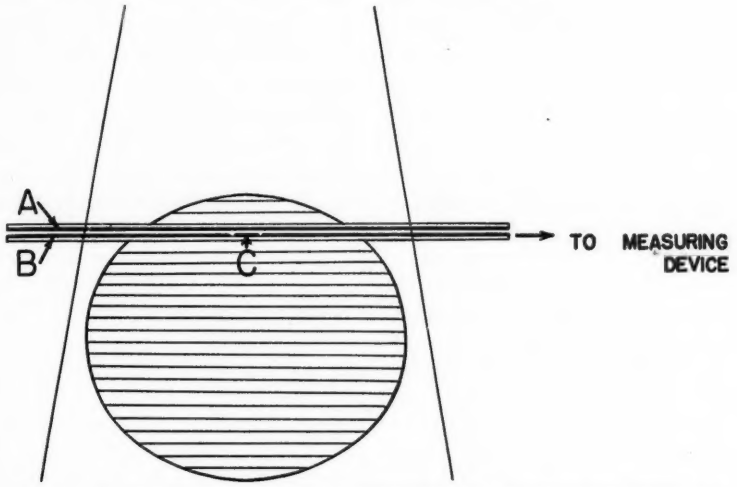

Fig. 2. Modification of extrapolation ionization chamber for the measurement of depth doses in a laminated phantom of the same shape and size as a given part of the human body.

$$D_b = D\,q = D_r\,f\,q,$$

in which D is now expressed in a unit representing the same number of ion pairs per gram of air as the roentgen (1.62×10^{12}). D may well be called the "tissue dose" and the unit the "tissue roentgen." It should be noted that the roentgen and the tissue roentgen have only one thing in common, namely, the number of ion pairs per gram of air. The conditions under which quantities of radiation must be measured in order to be expressed in roentgens, are set forth in the definition of the unit. The conditions under which quantities of radiation must be measured in order to determine the tissue dose are those which obtain in the biological material, during the irradiation, at the point where the biological effect is produced. They can then be expressed in "tissue roentgens."

Having presented the general method of attack somewhat in detail, it suffices to outline the necessary special procedures to be followed in special cases. In Figure 2 is shown schematically the case in which we wish to determine the tissue doses at different levels in a mass of tissue of the cross-

section shown. It is convenient to have the plate of the extrapolation chamber which carries the collecting electrode in one unit, with the wire connecting the electrode to the current measuring device properly insulated and shielded within the plate itself. The plate should be of organic material of approximately unit specific gravity, and should be a good electrical insulator. It should be thin. (The "Lucite" and "Styrol" electrodes mentioned previously fulfil these requirements, but since they have not been tested, we cannot say as yet that they are satisfactory.) The design of the upper electrode depends on whether surface or depth dose is to be determined. In the latter case, extrapolation to zero air space is all that is necessary, and the initial thickness of the upper electrode is not important. In the figure, fairly thick electrodes are shown. As a first approximation, the part of the body in which the depth doses are to be measured may be reproduced in shape and volume by slabs of pressdwood, as shown. Measurements at different levels can then be made by placing the proper number of slabs above and below the chamber. Extrapolation to zero air space is not always necessary, but this should be determined by experiment. If greater accuracy is desired it is necessary to reproduce in the phantom bones, air cavities, differences in tissue densities, etc., as they are in the part of the body under consideration. It is possible, but not very convenient, to use slabs of tissue from a frozen cadaver.

The extrapolation chamber of the type described so far is useful for measurements applicable to x-ray and telecurie therapy. In radium therapy the source is more often placed in body cavities or within the pathological tissues. In such cases the therapeutic effect is expected in the immediate vicinity of the source, and it is necessary to determine the dose at short distances therefrom. In Figure 3 is indicated the extrapolation method applicable to the case of a radium needle. A thin celluloid test tube, *T*, forms the inner electrode of the chamber. After coating its (outer) surface with India ink or "acquadag," two very narrow grooves are scratched in it with a sharp tool in the lathe. Thus a narrow band of the conducting surface is insulated from the rest, and forms the collecting electrode, *C*, which is connected to the measuring device through the wire, *W*. A second thin celluloid test tube of larger diameter than the first is coated with ink on the inside and forms the outer electrode, *O*. The two electrodes are mounted concentrically by means of the insulating rings, *I*. The conducting surfaces of the inner cylinder adjacent to the collecting electrode are connected to earth as shown, and serve the purpose of guard rings as well as that of providing a radial electric field. The volume in which the ionization is measured is determined by the area of the collecting electrode and the thickness of the air space between the test tubes. The radium needle, *Ra*, is placed in a narrow celluloid tube, *A*, attached to the smaller test tube as shown. The needle can be moved up or down depending on the longitudinal position at which the ionization is to be determined. Through tube *A*, filled with water, contact is made with the lower guard ring by means of the conductor *G*. The water and ground connection in this case also serve the purpose of removing any charge which might accumulate on the needle on account of the emission of primary or secondary electrons. Water (or water and ground tissue, if desired) is placed in the inner test tube and around the outer test tube, to provide the proper absorbing and scattering conditions. Extrapolation to zero air space is carried out by using outer electrodes of different diameters. It is desirable to obtain readings with very thin air layers since the inverse square law in this case has considerable influence. We have not made measurements with a chamber just as described here. However, with similar ones we have found an appreciable difference in the ionization current according to whether the outer electrode was charged positively or negatively. The difference is due to the excess of electrons leaving the collecting electrode. This

effect must be taken into account in determining the ionization in the (narrow) air space. The correct value of the ionization current is the average of the currents measured with positive and negative charges on the outer electrode.

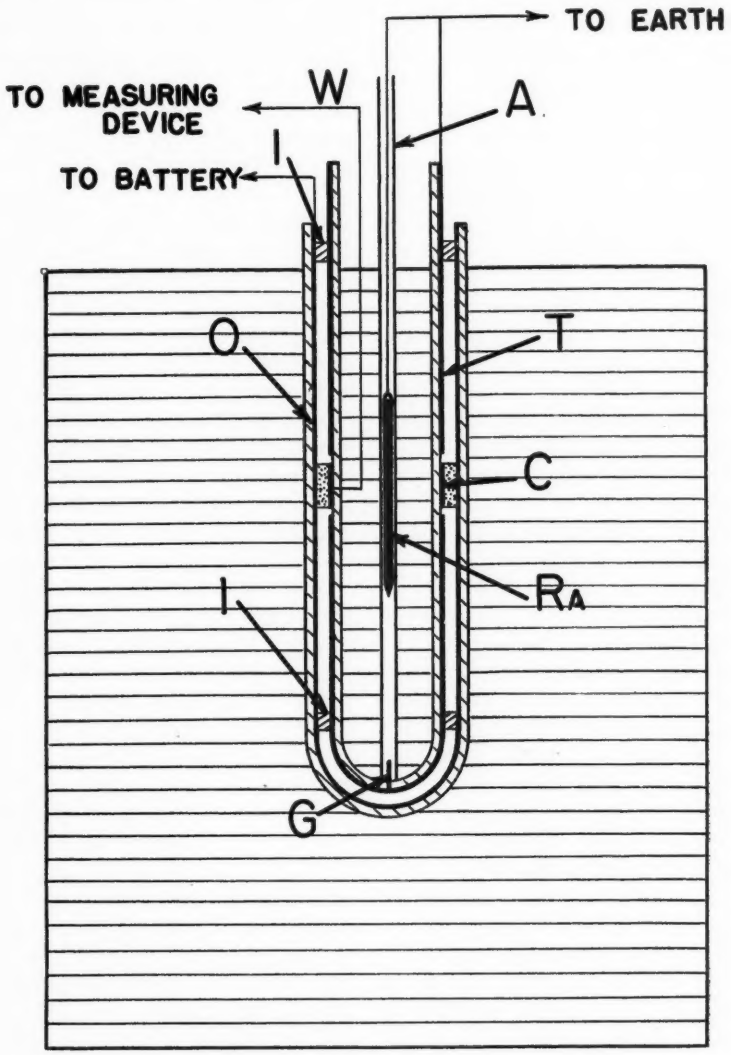

Fig. 3. Extrapolation ionization chamber for the measurement of tissue doses in interstitial radium therapy.

It is apparent that the determination of tissue doses by this method in the case of a radium needle or tube is a long and tedious process. So far we have not investigated the distribution of radiation around the source by this method, but we have made exploratory tests and we are sure that no serious practical difficulties will be encountered. Since in practice it is not essential to know the dose at distances from the source shorter than several millimeters, the smallest chamber used need not be less than one centimeter in diameter. This reduces the mechanical difficulties of cham-

ber construction. By suitable modifications of the two types of extrapolation chamber described here it is possible to determine the tissue doses in terms of the air ionization which would be produced at any point in an irradiated tissue, for all methods of radiation treatment used to-day.

In certain biological experiments very small test objects, such as *Drosophila* eggs or tumor fragments, are often irradiated in free air. Great care must be exercised in the measurement of tissue dose in such cases, particularly when gamma rays or supervoltage x-rays are used. One may determine the ionization at a certain point in atmospheric air by using thimble chambers of different wall thicknesses and extrapolating to zero wall thickness. In general this is a very difficult procedure. One must be able to eliminate not only the influence of the wall but also the influence of any material placed near the point in question in the process of making the measurements. How small the minimum wall thickness must be in order to permit extrapolation with reasonable accuracy, depends on circumstances—particularly on the range of the secondary electrons. In the case of gamma rays, measurements made with different chambers have not given us very consistent results, but we have not made a determined effort to overcome the difficulties since the problem is of no great interest. The important point to bear in mind in this connection is that the ionization produced in air at a certain point in a beam of radiation is not necessarily a measure of the tissue dose in a biological material placed at the same point, however small it may be. Each case presents a special problem which should be analyzed carefully.

The advent of neutrons and the rapid improvements in the methods of production, bring to us, with increasing urgency, the problem of measuring tissue doses in this case. So far as we can see to-day the extrapolation method is the only one which will give the desired information. In this case the agents directly responsible for the ionization are recoil particles the nature of which depends on the material traversed by the neutrons. These high speed charged particles ionize any matter they traverse just as alpha particles and electrons do. Accordingly for convenience and as a first approximation we may take air as the medium in which the ionization is to be measured. However, it is of the utmost importance in the measurement of tissue doses of neutrons that the conditions under which the ionization in air is produced be exactly those which obtain in the biological material at the point where the biological effect is produced.[9] For this reason the construction of suitable chambers of the extrapolation type is quite difficult. Two alternatives suggest themselves: (1) to make the chamber of "synthetic" materials having the exact chemical composition (insofar as elements are concerned) of the tissues in question, and (2) to make the chamber in such a way that the walls consist of the biological material itself, in the shape, volume, etc., in which it is at the time of the irradiation. Both are possible and we expect to construct some such chambers and conduct experiments with them in the near future. We may point out at this time an incidental advantage of the extrapolation type of chamber, in the measurement of ionization produced by recoil particles which liberate a large number of ions per unit path. It is difficult in this case to obtain saturation current, but with small air spaces such as employed in the extrapolation chamber, the problem is simplified. If necessary one can make use of the procedure followed by Taylor and Mohler (4) in determining the saturation current in liquids.

The problem of measuring tissue doses in the case of neutrons has been mentioned at this time primarily for the purpose of discussing the matter of units. As was expected it has been found that neutrons produce biological changes. What this will lead to no one can predict, but it is

[9] A distinction should be made between the point at which the biological effect is produced and the point at which the biological effect manifests itself. The two are not necessarily the same.

certain that many biological experiments will be carried out in the near future. It is extremely important that the comparison of biological effects produced by neutrons and by the better known ionizing radiations (x-rays and gamma rays) be made under proper conditions. It may well be assumed for the present that ionization is at the bottom of all these effects. Hence the correlation of dose and effect may best be made (so far as we know to-day) by specifying the dose in terms of ionization. The tissue roentgen may be used as a unit of dose in the case of neutrons or any agent capable of producing radio-ionization directly or indirectly provided the ionization is measured under conditions which insure a proportionality factor which is independent of the quality or kind of the radiation between the ionization actually measured and that produced in the living material, at the point where the biological effect is produced. Since the tissue dose is the quantity of paramount importance in all biological applications of radiation, it is very desirable to have a universally accepted unit for it. Its definition might be as follows: The tissue roentgen is the quantity of any ionizing radiation capable of producing 1.62×10^{12} ion pairs per gram of air at a given point in a given medium under the conditions in which the radiation is to be utilized. It should be noted, however, that the definition is general enough to cover any effect which may be brought about by any agent capable of producing radio-ionization (referred to by the general term "ionizing radiation"), irrespective of the nature of the effect (biological, chemical, or physical). Therefore, by leaving out the word "tissue" this could very well replace the present definition of the roentgen and thus remove the limitations which prevent the use of the unit in many cases. The suggested change would extend the use of the unit to other types of ionizing radiation and would clarify the situation without introducing complications in the ordinary x-ray range. It would make it unnecessary to have a separate unit of tissue dose. The desirability of such a change in the definition of the unit, the final wording, and the exact magnitude to be adopted, are matters which can be settled only by international agreement. It is extremely important that the subject be studied carefully and leisurely from all angles before final action is taken.

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CHOLECYSTOGRAPHY

FURTHER OBSERVATIONS ON THE USE OF PITRESSIN AND EVALUATION OF OTHER PROCEDURES

By E. N. COLLINS, M.D., *and* JOSEPH C. ROOT, M.D., Cleveland Clinic, *Cleveland, Ohio*

FURTHER observations which have been made since our preliminary report (1) on the use of pitressin during cholecystographic examinations have resulted in the routine use of this pressor fraction of posterior pituitary extract whenever there are confusing shadows in the intestinal tract, provided no contraindications are present. Our experience with pitressin as well as with certain other procedures which increase the accuracy of cholecystography will be considered. Our routine method of combining cholecystography with the roentgen examination of adjacent organs will also be discussed.

Since the introduction of cholecystography by Graham and his co-workers in 1924 (2, 3), its importance in the diagnosis of dysfunction or disease of the gall bladder has become well established, but the technic of this procedure is still not standardized. Because of this lack of standardization, the clinician as well as the roentgenologist now insists upon knowing the details of the method used in order to judge its reliability.

From the roentgen standpoint, the diagnosis of disease of the gall bladder can be made from the cholecystographic evidence alone when it reveals the presence of gallstones, calcific deposits in the wall of the gall bladder, opaque bile in the gall bladder due to the presence of calcium carbonate bile (4, 5), or of neoplasms (6) in the gall bladder. However, unless the patient's history suggests the presence of these conditions, care should be taken in attributing the presenting symptoms to these causes unless abnormalities in adjacent organs are excluded. Normal cholecystographic findings do not necessarily indicate a normal gall bladder and non-visualization in the cholecystograms does not always indicate a pathologic gall bladder. Clinicians have been reluctant to place reliance on the cholecystographic findings when they did not adequately explain the cause of the patient's symptoms.

The clinical diagnosis of cholecystic disease is usually simple when the patient gives a history of one or more attacks of biliary colic, particularly if these have been associated with jaundice. In such instances, objective roentgen evidence for confirmation is obtained by cholecystography. In inflammatory diseases of the gall bladder, the physical examination usually offers no assistance unless the patient is examined during the acute or subacute phase of the process.

In the absence of a history of biliary colic, cholecystography is no less important but it must be combined with the roentgen examination of adjacent organs as well as correlated with the patient's symptoms in order to adequately explain the cause of the disability. In these instances the roentgen examination of adjacent organs often proves more valuable than cholecystography alone.

In this presentation we are chiefly interested in cases in which a characteristic history of biliary colic is absent, in which the roentgen examination of adjacent organs is combined with cholecystography, and in which the use of every important refinement in cholecystographic technic is needed in order to accurately determine the cause of the patient's presenting complaints. Soon after the introduction of cholecystography Nichols (7, 8) established the combined method of roentgen examination at the Cleveland Clinic, and these same procedures are used to-day, twelve years later. He has repeatedly emphasized the fact that, since the sympathetic nervous system through the superior and inferior mesenteric ganglia receives fibers not only from the gall bladder, but also from the stomach, duodenum, right kidney, ureter,

and colon, pain or distress in the right upper quadrant of the abdomen may be due to abnormality in any one or several of these organs. It is generally agreed that biliary disease is the most common *organic* cause of chronic gastro-intestinal symptoms in a middle-aged person. Routine autopsies, both in this country and abroad (9, 10), show that more than half the adults past 30 years of age had abnormal gall bladders and that approximately 20 per cent had gallstones, but the relatively low incidence of previous clinical evidence of biliary disease in these cases makes one question the advisability of prescribing surgery on the basis of cholecystographic evidence alone (11). It is well known that the best results from surgery of the gall bladder are obtained in those patients who have had definite biliary colic, and operations on the biliary tract are now seldom advised unless there is positive clinical as well as cholecystographic evidence.

It should be more generally recognized that the patient's gastro-intestinal symptoms may originate in the urinary tract. Urinary calculi as a cause of gastro-intestinal symptoms, particularly nausea and vomiting as well as pain, is well known. Patients have been operated upon for appendicitis or even intestinal obstruction when the trouble was in the urinary tract. Normal findings on routine urinalyses do not exclude abnormality in the urinary tract. In our cases of hypernephroma, the incidence of hematuria has not been greater than 50 per cent, and 34 per cent of our patients with hydronephrosis have had previous abdominal operations without relief of symptoms. Although hydronephrosis due to aberrant blood vessels apparently is a rare condition, it may simulate biliary disease, and almost invariably normal urinary findings are present. In 19 per cent of a group of patients with kidney tumors, there was no history indicative of disease of the urinary tract.

The interpretation of so-called gall-bladder dyspepsia or gaseous dyspepsia, as described in text-books, when it is not associated with definite attacks of biliary colic, is open to question. Although patients who give a history of biliary colic often have functional disturbances in the gastro-intestinal tract, Palmer (12) believes that, in the absence of this history, so-called gall-bladder dyspepsia is in reality independent of the gall bladder and that it is not unlike the dyspepsia which occurs in patients who are not afflicted with cholecystic or other forms of organic disease. In our experience, the most frequent cause for these indefinite symptoms is a functional disturbance in the colon, particularly in patients who have constipation or diarrhea, or one alternating with the other for a long time, and in whom catharsis, irritating enemas, or neurogenic factors may be important. When a complete examination excludes the possibility of organic disease, and this frequently includes examination of stools and proctoscopic examinations, we ascribe the condition to the "irritable colon syndrome," a term originated by the late B. W. Sippy.

In dealing with a patient who has indefinite gastro-intestinal symptoms, accurate diagnosis is usually made by a process of exclusion. Our aim has been to make the examinations which will be of the greatest practical benefit to the patient per unit of available time, and this generally means an investigation limited to two or three days. Our routine procedure has been to use the newer developments in cholecystography, the single or double oral method of administration of the dye, and at the same time complete the roentgen examinations of the stomach, small intestine, and colon. Prior to the administration of the cholecystographic dye, plain films of the gall-bladder area and urinary tract are made routinely. If abnormality in the latter is found, excretory urograms or retrograde pyelograms are completed before the administration of the barium meal. The time factor is the same as that required to complete the fractionated or multiple dose method of cholecystography alone.

In attempting to standardize cholecys-

tographic procedures, we believe the following features should be considered:

1. After countless discussions relative to the merits of the intravenous *versus* the oral method of administering the dye, the oral method has had general adoption. This is the simpler method for both patient and roentgenologist, and from a practical standpoint very little if any accuracy in end-result is sacrificed. However, the intravenous method combined with determination of liver function, using "isoiodeikon" (sodium phenoltetraiodophenolphthalein), as described by Graham (13), has been found important in dealing with a patient having obvious biliary disease, because of the added information relative to surgical risk.

2. The administration of multiple doses of the dye produces greater density in the visualized gall bladder than does the single dose, and it makes non-visualization of greater significance, without harming the patient.

3. The administration of large amounts of sugar and other carbohydrates preceding and during the examination facilitates the excretion of the dye by the liver, thereby adding greater significance to the cholecystographic findings.

4. One ounce or less of a mixture of egg yolk, lecithin, and glycerine, as recommended by Levyn (14), has been found to be as efficacious as the fat meal in emptying the gall bladder, and it has not interfered with the roentgen examination of the stomach or intestine on the same day that the cholecystograms are made.

5. The use of pitressin in the elimination of confusing shadows in that part of the intestinal tract which may lie over the area of the gall bladder has precluded the necessity for re-examinations in such instances. It has also made possible the use of the multiple dose oral method of cholecystography on the same days that the barium meal examinations of the stomach and small intestine or the barium enema examinations of the colon are made.

6. The importance of radiographic technic is well recognized but is too often neglected. Kirklin (15), Barclay (16), and many others emphasize this feature. Adequate penetration of the gall-bladder area, using the minimum of kilovoltage as well as the shortest possible exposure time to eliminate motion, are the most important factors. Milliamperage higher than that commonly used as well as the use of a high speed Bucky diaphragm are desirable. The technic should be standardized so that accurate results may be repeated at will, and much depends on the interest of the radiographer and the care used in taking the films, as well as his skill.

Sandström (17, 18) introduced the "multiple" or "fractionated" method of cholecystography. He stated that "phenolphthalein preparations, once introduced into the system, circulate for a rather long time in an enterohepatic cycle. After being eliminated through the liver and its intermediary, the bile, they are reabsorbed through the intestines, and so on. By introducing orally during each phase of the cycle additional small doses of the salt one may obtain a more complete absorption." He administered orally 7 to 10 grams of sodium tetraiodophenolphthalein in two or three divided doses, allowing two or three days for the cholecystographic examination, and he found that greater absorption, resulting in greater density of the visualized gall bladder, was obtained without harm to the patient.

Sandström apparently allowed the patient to eat a mixed diet between the divided doses of the dye and so made no attempt to prevent emptying the gall bladder. Since carbohydrates had been shown to have no effect on the emptying time of the gall bladder in man (19), Whitaker and Ellsworth (20) modified the Sandström method by giving only carbohydrates between the two doses used in their "double oral" method. Whitaker (21) has since advocated that another carbohydrate meal be followed by a *third* dose of the dye if the roentgenograms at the end of 20 hours show no visualization of the gall bladder.

Stewart and Illick (22, 23) in their "intensified" oral cholecystography combine

the fractionated method of administration of the dye with the administration of large amounts of sugar to facilitate the excretion of the dye by the liver, allowing only carbohydrate foods until noon of the third day when a fat meal is given to empty the gall bladder.

In our experience the use of the "fractionated" or "multiple" dose method is important when the cholecystographic findings are questionable, particularly when there is non-visualization by the single dose method. The single dose method, in our hands, has proved adequate in 90 per cent of the cases. We find that the greatest inaccuracy of cholecystography has been in those instances in which there is normal visualization of the gall bladder when chronic cholecystitis of clinical importance actually exists. We must remember that a gall bladder which is full of calcium-type stones often functions normally with cholecystographic dye, and we are convinced that the presence of calcium-type stones denotes cholecystitis. It would seem that the use of the smallest adequate amount of dye would reduce the inaccuracy mentioned.

In his "rapid" cholecystography, Antonucci (24) demonstrated the value of using glucose with the intravenous method. Ten minutes after the intravenous injection of 125 c.c. of a 40 per cent solution of glucose, the dye was injected. This, in turn, was followed by the subcutaneous injection of 24 units of insulin. Visualization of the gall bladder was usually obtained within half an hour following the injection of the dye, and the maximum intensity was reached in two hours. It was Antonucci's opinion that glucose played an important part in the utilization of the dye and that the absorption of the dye in the liver necessitated the presence of glucose either in the blood stream or as converted from glycogen in the tissues, if the former became exhausted. This coincides with our experience. We believe the more carbohydrates that are given during the cholecystographic procedures the better.

Cholecystograms which are taken after giving a fat meal may show the presence of gallstones or neoplasms which are not apparent in former cholecystograms, but so far as function is concerned, we must remember that the gall bladder must empty in order to fill with the cholecystographic dye and that normal visualization of the gall bladder, as compared with plain films signifies a functioning gall bladder, so far as cholecystography is concerned.

CHOLECYSTOGRAPHY AND DETERMINATION OF LIVER FUNCTION

Blomström and Sandström (25) supplemented cholecystography with the bromsulphalein test in 68 cases as a means of determining the liver function in the event of non-visualization of the gall bladder after the administration of the dye. A high retention of bromsulphalein, over 40 per cent, excluded the possibility of visualization of the gall bladder because of liver damage. A low retention, however, below 25 per cent, indicated that obstruction was located outside the liver parenchyma.

Graham (13), in 1933, demonstrated the value of combining intravenous cholecystography with determination of liver function by the use of "iso-iodeikon" (sodium phenoltetraiodophenolphthalein). He found that a knowledge of the amount of this dye which was excreted by the liver was of considerable value in estimating the risk of performing operations on the biliary tract. In addition, it was of assistance in the interpretation of the cholecystograms. By delaying operations until the proper medical treatment resulted in a reduction of high dye retentions to normal, the accuracy of the interpretation of the cholecystographic findings was increased, and the mortality rate for operation on the biliary tract could be reduced materially.

THE USE OF PITRESSIN DURING CHOLECYSTOGRAPHY

One of the handicaps to accurate interpretation of cholecystograms is the presence of confusing densities, such as gas shadows, in the intestinal tract. Repeated examinations may be necessary be-

fore an accurate diagnosis can be made. In our experience, the use of cathartics and enemas has proved not only inadequate,

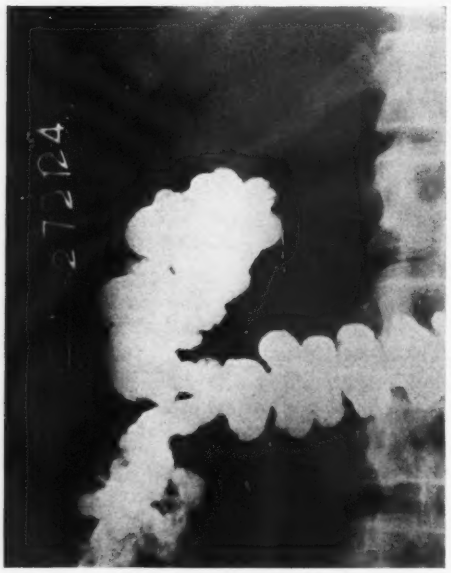

Fig. 1. Gall-bladder area obscured by barium in the colon.

Fig. 2. A normally functioning gall bladder visualized after administration of pitressin.

but it has actually resulted in greater difficulties than were present before their administration in many instances. We have found the use of pitressin, the pressor fraction of posterior pituitary extract, effective in solving this problem, and its use is a simpler procedure, requires less time, is less troublesome to the patient, particularly if he is not in a hospital, and it has not been attended by unpleasant reactions. However, because of its stimulating effect on the musculature of the gastro-intestinal tract as well as its vasoconstrictor effects, it has not been used when there is danger of perforation or mechanical obstruction in the gastro-intestinal tract or in cases in which there is evidence of cardiovascular disease. We do not use pitressin in the presence of advanced hypertension, and since we have noted a drop in blood pressure in 60 per cent of our cases in which it has been used, it is not given to a patient whose systolic blood pressure is below 100 mm. of mercury.

We have used pitressin in 500 cases, this number being about 10 per cent of the total number of cholecystographic examinations made during that period of time. There is no need for its use routinely and if it is given in the presence of one or more of the above mentioned contra-indications the potential danger is obvious.

Effective results, *i.e.*, the elimination of confusing shadows in the intestinal tract, were obtained in 90 per cent of the cases. Figure 1 illustrates a case in which the second dose of dye was given the night following the routine examination of the stomach. It will be noted here that the entire gall-bladder area is obscured by barium in the colon, and no information about the function could be obtained by this cholecystogram. The patient was given 1 c.c. of pitressin and a second film was made 45 minutes later. The barium was evacuated from the colon, and we are now able to see in Figure 2 a normally functioning gall bladder.

In approximately 75 per cent of this group one or more stools occurred within 30 minutes.

Blood pressure readings were made before the administration of the pitressin and one hour after the injection in 300 cases, and in certain instances these readings were made every five minutes during the hour. There was a drop in the blood pressure in 60 per cent, and of this number there was a drop in both the systolic and diastolic pressure in 45 per cent. The average decrease for both the systolic and diastolic pressures was 12 mm. of mercury. An increase in blood pressure was experienced in only 20 per cent of the patients, and of this group there was an increase in both the systolic and diastolic pressure in 8 per cent. The average increase in the systolic pressure was 9 mm. and the diastolic pressure was 12 mm. of mercury.

The technic is merely the intramuscular (deltoid) injection of one ampule, 20 pressor units, when the first cholecystograms show confusing shadows in the intestinal tract. Additional films are then made one hour later. There has been no interference with the roentgen examination of the stomach, small intestine, or colon on the same day that pitressin is used.

This procedure is now our method of choice for the elimination of the confusing shadows mentioned and it is used routinely in such instances, provided no contraindications exist.

METHOD OF EXAMINATION

In patients who give a history highly suggestive of biliary colic, we obtain confirmatory evidence by making cholecystographic examination by the oral method, and this is combined with a roentgen examination of the stomach and duodenum to exclude the possibility of a penetrating ulcer in the posterior wall of the duodenum which may cause symptoms suggesting biliary disease in the absence of jaundice. Symptoms due to a neoplasm of the stomach have been ascribed to biliary disease.

A plain film of the urinary tract is always made at the time the preliminary plain films of the gall-bladder region are made. If the roentgen findings in the urinary tract are positive or suggestive of abnormality the patient is referred to the Department of Genito-urinary Diseases for further examination before cholecystography is completed. Intravenous or retrograde pyelography may be indicated. There may be abnormality in the urinary tract as well as in the gall bladder, or the symptoms actually due to the former may be highly suggestive of the latter.

In rare instances, a calcification is visualized which may be either in the gall bladder or in the pelvis of the right kidney. As pointed out by Nichols, a consideration of the physics of the technic makes the differentiation simple when the characteristics and position of the shadows are compared in both the gall-bladder film, made in the postero-anterior position, and the urinary tract film, made in the anteroposterior position. The closer the object is to the film the smaller and more distinct it will be.

Various forms and amounts of the dye and various modifications have been used with the dye, but, in our hands, the plain dye (sodium tetraiodophenolphthalein) taken in grape juice or other fruit juices has caused the least discomfort and has given the most satisfactory results from the standpoint of absorption. The one ounce bottle given to the patient contains 5 grams of the dye, one and one-half drams of paregoric, and distilled water, prepared on the day of administration. Immediately after the six o'clock high-carbohydrate-fat-free meal the patient shakes the bottle, empties its contents into a glass containing the fruit juice, stirs thoroughly, and drinks it all quickly. The following morning black coffee or clear tea with as much sugar as desired are allowed. Emphasis is placed on the ingestion of as much sugar as possible at all times during cholecystography.

The first cholecystograms are made 14 hours after the ingestion of the dye. If these films are satisfactory, as is the usual case, the roentgen examination of the stomach and duodenum is done without further delay. If the 14-hour cholecystograms show insufficient or non-visualization of the gall bladder, the latter ex-

amination is delayed until 16-hour cholecystograms are made. If questionable shadows are present, or if the gall bladder is obscured by shadows in the intestinal tract, use is made of the lecithin mixture or pitressin or the two procedures may be combined. If the findings are still questionable, particularly if there is insufficient or non-visualization of the gall bladder, a second dose of the dye is given the second night, even though the roentgen examination of the stomach and small intestine is made on the same day the cholecystograms are made. The 6-hour gastric retention film often shows excellent visualization of the gall bladder. We believe that a second dose of dye should always be given on the second night of the examination if the gall bladder is not visualized initially or if the density is so slight that the presence of non-opaque calculi cannot be determined with a high degree of accuracy. A second dose should also be used routinely if the patient happens to be of the small group that may vomit the dye before there is sufficient time for its absorption, resulting in non-visualization of the gall bladder. We have found that in this group the second dose is well tolerated and it is a rare occurrence for the dye not to be retained.

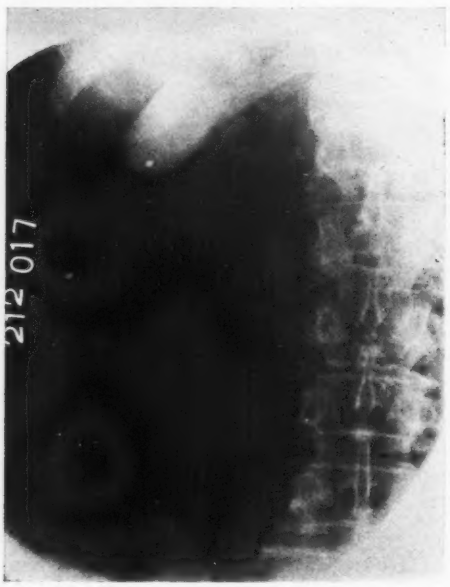

Fig. 3. Questionable opaque calculus in gall-bladder area.

Fig. 4. The gall bladder contracted after administration of lecithin mixture. Questionable shadow now outside of the gall bladder.

Although the lecithin mixture is frequently used, pitressin or a second dose of the dye has not been indicated in more than 10 per cent of our cases. We find that the gall bladder has diminished at least 50 per cent in size one-half hour after the oral administration of five drams of the lecithin mixture. This amount has not been found to interfere with the roentgen examination of the stomach one-half to one hour after its administration. The use of this mixture has supplanted the use of the fat meal in our hands and, although not used routinely, it has been very helpful in determining the significance of questionable shadows in the area of the gall bladder. Figure 3 shows a small opaque calculus in the gall-bladder area, which, at this time, cannot be excluded as an opaque calculus. The patient was given four drams of the lecithin mixture, and the second film was made one-half hour later. Figure 4 shows the gall bladder in a contracted state with the suspicious shadow outside the gall-bladder

area. The fat meal may be given during the course of the combined gastro-intestinal examination, four to six hours after the stomach examination, but the possibility that the gall-bladder area will be obscured by barium in the intestinal tract is present.

TABLE I

Cholecystographic Findings	Number of Cases	Pathologic Findings				
		Chronic Cholecystitis				
		With stones	Without stones	Stone, cystic duct	Ca. carb., bile, and stones	Grossly normal
Normally functioning gall bladder without stones (negative)	5		4	1		
Normally functioning gall bladder with evidence of adhesions	1		1			
Gallstones in a normally functioning gall bladder	37	35	2			
Gallstones in a poorly visualized gall bladder	29	27	2			
Poorly visualized gall bladder without evidence of stones	6		6			
Gallstones in non-visualized gall bladder	31	31				
Non-visualized gall bladder without evidence of opaque stones	40	33	6			1
Non-functioning gall bladder with calcium carbonate, bile, and stones	1				1	

In the large group of patients who give an indefinite history of digestive disturbances, motility studies of the small intestine as well as barium enema examinations of the colon are added to the procedures mentioned. *This constitutes our routine gastro-intestinal series examination.* Those patients who are to have a colon examination on the following morning take from one to two ounces of castor oil after the six-hour gastric retention film is made.

In instances in which a second dose of the dye is given on the second night, even though barium meal examinations of the stomach and small intestines have been done, the use of pitressin is often needed in order to satisfactorily visualize the gall bladder the following morning. No cathartics are given when further cholecystographic procedures are to follow. Methods used in the roentgen examination of the colon have been published elsewhere (26).

We believe that the fractionated or multiple dose method of administering the dye is not necessary as a routine procedure in cholecystography. As stated, the examination of organs adjacent to the gall bladder is often more important in establishing the cause of the patient's presenting symptoms than cholecystography alone. Time and expense to the patient are important factors.

RESULTS

Establishing the accuracy of cholecystography is, of course, difficult, because relatively few of the patients in whom these examinations are made have abdominal operations. However, our findings in abdominal operations during the past five years have coincided with the cholecystographic findings in either a positive or negative way in 95 per cent of the cases. In a series of 150 patients having cholecystectomies, the cholecystographic findings were accurate in 93 per cent. The cholecystographic examinations in this series of cases, in the majority of instances, were made before the employment of the lecithin mixture, the occasional second dose of dye, and before the use of pitressin. In Table I is a summary of the cholecytographic

and pathologic findings in parallel groupings.

In a consideration of the errors, there were five cases on the negative side in which normal cholecystographic findings had been obtained and little gross evidence of abnormality of the gall bladder was found at operation, but the microscopic diagnosis was chronic cholecystitis. In four of these, there were no stones; in the fifth case there was a stone in the cystic duct but none in the gall bladder. The clinical significance of a microscopic diagnosis of chronic cholecystitis in the absence of definite gross pathologic changes is disputed by many authorities.

On the positive side, a diagnosis of gallstones was made in four instances, but operation did not confirm this; however, pathologic gall bladders were found. Two of these four patients had poorly visualized gall bladders by cholecystogram which apparently indicated diminished function. Another positive diagnostic error was made in a case of non-visualization in which the gall bladder was found to be grossly normal at the time of operation, and the appendix was definitely pathologic. This type of error is bound to occur since conditions extrinsic to the gall bladder are known to produce non-visualization of the gall bladder by cholecystography.

EVALUATION OF CHOLECYSTOGRAPHIC FINDINGS

Statistics relative to the accuracy of cholecystography are generally based on operative findings. Because of this, the cholecystographic evidence alone is open to question. In most instances there is positive clinical as well as positive cholecystographic evidence of biliary disease before operation. However, Kirklin and Blake (27) have summarized the cholecystographic evidence in patients who have not had abdominal operation but who did have a final clinical diagnosis of cholecystic disease. They found that the cholecystographic data coincided with the clinical diagnosis in approximately 90 per cent, which approaches the accuracy of cholecystography in cases proved by operation.

We believe the following are important features to be considered in a practical evaluation of cholecystography:

A gall bladder normally visualized by cholecystography may be pathologic, even though in most instances it denotes a normal gall bladder. Convincing clinical evidence is necessary in order to justify surgery on the grounds of biliary disease if the cholecystographic findings are normal.

On the other hand, gall bladders which are full of calcium-type stones commonly function normally with the cholecystographic dye. In the absence of gallstones, the routine use of multiple doses of dye should logically increase the error in diagnosis so far as normally functioning gall bladders by cholecystography alone are concerned. There must be many patients who have symptoms due to chronic cholecystitis without stones who have normal cholecystographic findings. Giving the smallest possible adequate dose of cholecystographic dye should decrease the error in the roentgen interpretation of these cases. The patient should not be told that his gall bladder is normal on the basis of cholecystographic findings alone.

Non-visualization of the gall bladder without evidence of opaque calculi usually indicates a non-functioning gall bladder containing calculi of the cholesterin type, often blocking the cystic duct. But consideration must be given to the possibility of other causes of non-visualization, such as diseases of the liver or diseases in adjacent organs which may cause reflex disturbance in the dye-concentrating ability of the gall bladder or dysfunction in the sphincter of Oddi. An active duodenal ulcer may cause non-visualization. In other words, non-visualization does not necessarily indicate a pathologic gall bladder, and such a diagnosis should not be made unless there is a suggestive history of biliary disease and roentgen examination of adjacent organs reveals no evidence of abnormality. The multiple dose method of administering the dye, combined with

a large intake of sugar, is definitely indicated in the event of non-visualization. Added doses at each phase of the enterohepatic cycle usually are more effective than a re-check single dose examination at a later date unless there is abnormality outside the biliary tract causing reflex disturbances which are relieved in the meantime.

CONCLUSIONS

1. In a group of 150 patients who have had cholecystectomy, the operative findings coincided with the cholecystographic findings in either a positive or negative way in 93 per cent of the cases.

2. The use of a single dose of dye has been found adequate in 90 per cent of our cholecystographic examinations. In the event of non-visualization or questionable findings with the single dose method, a second dose of dye is given the second night.

3. The use of pitressin has been found effective in the elimination of confusing shadows in the intestinal tract. Its routine use has not been necessary. During 5,000 cholecystographic examinations it was used in approximately 10 per cent of the cases. Contra-indications to its use have been established.

4. The routine use of the combined method, *i.e.*, combining the roentgen examination of adjacent organs with cholecystography, has proved valuable during 12 years of experience. The extent of the examinations of adjacent organs has been determined by the presence or absence of a history of definite biliary colic in each case. Abnormal cholecystographic findings do not necessarily explain the cause of the patient's abdominal symptoms.

5. The use of the lecithin mixture to supplant the fat meal and the use of pitressin when indicated has made possible the completion of the combined method of roentgen examinations, using either the single or double oral method of cholecystography, in the time required to do the multiple dose method of cholecystography alone.

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FRACTURE OF THE ATLAS OR DEVELOPMENTAL ABNORMALITY?

By H. F. PLAUT, M.D., *Cincinnati, Ohio*

THE following is the report of a patient seen after an automobile accident, July 17, 1936. A colored girl, student, 18 years of age, was admitted to the St. Philip's Hospital, Medical College of Virginia, Richmond, Va. (Neurosurgical Department, service of Dr. C. C. Coleman), about fifteen minutes after she had jumped from the rumble seat of a moving automobile. She had projectile vomiting about ten minutes after admission. She was unconscious, showed a soft swelling of lemon-size over the left parietal region, and there was oozing of blood from the left ear without demonstrable abrasion in the auditory canal. The pupils reacted to light and were equal in size. No rigidity of the neck was found.

Immediate x-ray examination revealed a definite fracture line through the parietal bone on either side (see Fig. 3). The fracture line followed the lambdoid suture rather closely on the right side and was situated more anteriorly on the left with another fracture line extending through the region of the sella on the left side. This fracture line apparently did not separate the sphenoid but the bone overlapping the sphenoid. The head was seen to be lower than usual, as if the lower part of the occiput was pressed against the arch of the axis, mashing that part of the atlas-ring in between. In the further course no neurological changes or deafness were observed.

Three days later another roentgen examination was made. In the lateral view there was a large bilateral gap in the posterior arch about 8 mm. wide (see Fig. 4). The axis was in normal position. On July 27 the patient was discharged, on her request, with a Thomas collar.

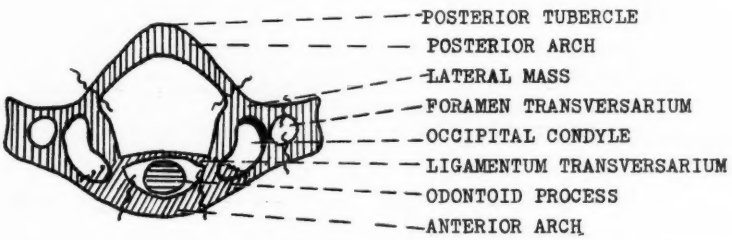

Fig. 1. Diagram of the human atlas, showing its morphological parts and fracture sites. The greater part is formed by the basidorsals; the basiventrals form a ring surrounding the odontoid process of the axis and composed of the bony anterior arch, including the anterior ends of the condyles, and the fibrous ligamentum transversarium. The odontoid process is the separated interventral of the atlas. (*Modified after Gadow.*)

DISCUSSION

A case reported by Lawrence and Anderson (13) has many similar features. Their female patient was sitting in an automobile when a street car bumped into it. Her head jerked backward with some violence. On account of the x-ray findings, a diagnosis of fracture of the posterior arch of the atlas was made by the attending surgeon. This was also the first impression of the authors. When re-examined for medico-legal purposes ten days after the accident, the patient still complained about stiffness in the neck. A space about one-half inch wide, separating the undisplaced portion of the posterior arch from the anterior portions of the vertebræ, was noted. No fragments were seen in the gap. The

diagnosis then was altered to one of rare developmental abnormality. Objective neurologic changes were not mentioned.

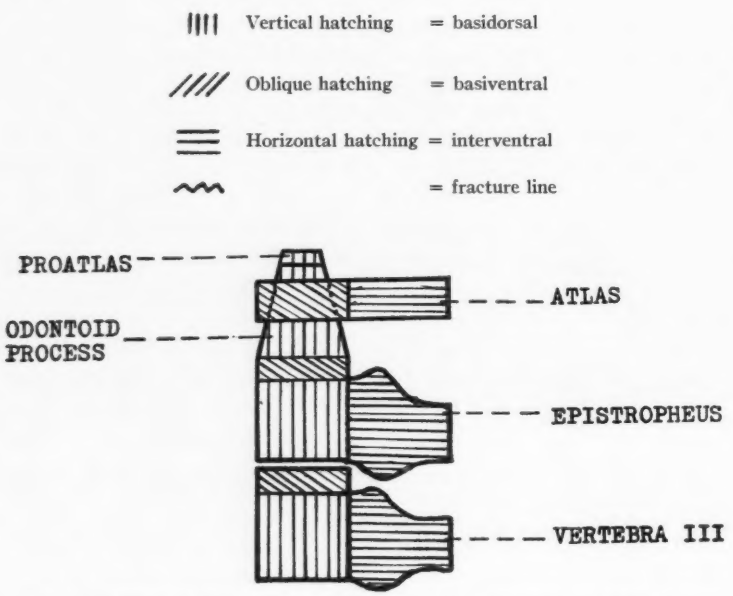

Fig. 2. Scheme of first three vertebræ. The first vertebra, or atlas, is composed of basidorsal and basiventral elements. The odontoid process of the epistropheus, which is seen passing through the first basiventral, is the interventral of the atlas. The tip of the odontoid process is formed by the interventral of the proatlas. The second vertebra, or epistropheus, consists of the fused and ossified basidorsal, interventral, and basiventral, to the last of which the odontoid process is also fused. The third vertebra is a typical vertebra formed of the co-ossified basidorsal and interventral, with the basiventral forming the intervertebral fibro-cartilage between it and the epistropheus. (*After Gadow.*)

It is interesting to study the facts concerning these two cases in order to discuss the differential diagnosis of injuries and anomalies of the atlas. Strassmann describes a transverse rupture of the trachea, and Romanese (14) a fracture of the third cervical vertebra, both fatal lesions without any signs of direct force to the neck, alone due to a backward jerk of the head when the individual was hit from behind by an automobile. The relaxation of the musculature at the moment of the unsuspected violent trauma is made responsible for these surprisingly severe injuries. Judging from the description of the accident in Lawrence's case, the street car probably hit the automobile from behind. It would be desirable to know if the head struck any part inside the car and if there were any skin lesions, swellings, or other signs of direct trauma.

At the first examination of our patient we had the impression that her upper neck was shorter than usual, although its rotated position was taken into consideration. The skull appeared to be pressed into the gap of the posterior arch of the atlas against the axis. Because of the overlapping of the mastoid process it was rather difficult to make a definite decision as to the presence of fragments but there seemed to be more calcified tissue than was due to the mastoid. The fact is striking that no fragments of bone were visible in the wide gap of three days and ten days, respec-

tively, after the accident to the patient under discussion and Lawrence and Anderson's patient.

Fig. 3. Roentgenogram of skull, taken immediately after accident, with upper cervical vertebræ in rotated position.

One may assume that the prevailing cause of fractures of the atlas is a violent pressure of the skull against the cervical spine when fixed in a rather straight position. The character of the trauma in our patient could quite well produce a fracture of the atlas. A displacement of the fragments does not necessarily take place. A review of the literature about fractures of the atlas, accompanied by excellent roentgenograms, fails to show similar changes to those described by Lawrence and in this article. There were reports of fractures into numerous pieces, but no gaps of this extent. On the other hand, there are no such formations mentioned among the variations and developmental abnormalities of the atlas.

The atlas ossifies from three main centers. Two, one for each lateral mass extending into the posterior arch, are present at birth and *unite posteriorly* in the third to fifth year of age. The third center appears around the first year of life in the anterior arch and unites with the two lateral centers in the fifth to ninth year. A separate ossification center may be present in the region of the posterior tubercle and possibly a groove, occasionally noted in this region, is due to missing of this center.

Gap formations illustrate the tendency of the human atlas to undergo further regression. The overwhelming majority of the gaps in the posterior arch lies near the midline; very rarely are they seen near the lateral masses. The width ranges from a fissure to about ten millimeters, and even nearly complete absence of the posterior arch is known. In the anterior arch gap formations are less frequent. During life, interruptions of the atlas due to persisting cartilage seams or gap formations were demonstrated roentgenologically by Renander (11), Arkussky, Engländer (6), and Lorey (12). Until 1932 Geipel (7) found, among 1,136 spines, 35 cases with fissures and gaps in the atlas ring. He had an opportunity to examine part of the specimens histologically and observed firm tracts of connective tissue leading from one end of the gap to the other, originating from the periosteum and inserting at the bone. Another connection of the two

ends was seen in one of those rare cases of entirely missing posterior arch: a flaccid band formed by the posterior membrane

Fig. 4. View of cervical spine, taken three days after accident, in lateral direction.

(a tense band would narrow the canal too much to allow sufficient space for the cord). *However, no bone formation could be demonstrated in any of these fibrous strings.*

Decalcification.—Another point has to be borne in mind: Lack of callus and pseudarthroses after fractures of the three upper cervical vertebræ were seen by quite a few authors. One of our patients, whom we had the opportunity of re-examining roentgenologically eight months after his bilateral fracture of the atlas, also showed this phenomenon. Spontaneous dislocations of the atlas in children have been not infrequently reported in recent years after inflammations of the upper respiratory tract and neighboring tissues (15). These luxations occurred as early as from one to two weeks after the upper respiratory infection and were found to be due to loosening of the attachments of the transverse ligament. From these cases we likewise must assume that an exceptional opportunity exists for decalcification.

It seems to be very difficult to do justice to the remaining possibility of a tear or break in a mostly cartilaginous posterior arch, because the roentgenological signs are few. A dislocation of the separated posterior piece of bone, however, would speak very much in favor of a traumatic lesion. While in other regions of the body clinical findings may help, they certainly disappoint in a case like ours. As a rule a fracture of the skull overshadows the coinciding fracture of the atlas in the clinical picture and decides the final result.

Mortality.—For fractures of the atlas, Jefferson (4), states that of 32 cases reported from 1900–1927 only six patients have died. The mortality in recent years has been very low. Among the 29 cases which were added by a review of the literature and our own cases, there were only three casualties, so that one's impression at present is that atlas fracture, though fraught with the possibility of danger, is by no means always fatal.

As to differential diagnosis it would have been of immense value for us to be able to follow the subsequent course, not to speak of a roentgenogram made before the accident. However, we did not succeed in our efforts to induce the patient to appear for roentgenographic control.

CONCLUSIONS

The following table shows the reasons for one or the other diagnosis.

Fracture	*Abnormality*
History:	
No such malformations reported.	No such fractures reported.
Ossification center in posterior tubercle is inconstant and not reported in malformations due to arrest of development.	No clinical signs; no rigidity of neck.
Exceptional opportunity for decalcification in this region.	No fragments noted 3 days after injury.
Site of most frequent bilateral fracture.	No dislocation of posterior piece of bone.

Without satisfactory lateral roentgenograms taken before or immediately after the accident to demonstrate fragments, or at least such views taken several months thereafter for signs of reparation, it is hardly possible to make a reliable decision as to the nature of the findings. It is noteworthy that the changes were found only in two cases with definite and severe indirect trauma to the neck. For this last reason I would be more inclined to regard them as a bilateral fracture of the posterior arch of the atlas with hitherto unknown comminution. However, the facts are not absolutely conclusive without further study of the subject.

SUMMARY

A case out of a series of atlas fractures shows unusual width of bilateral gaps in the posterior arch, which raises the question of developmental abnormality. It is compared with the only similar case found in the literature with interesting medico-legal consequences, likewise seen after a severe indirect injury of the cervical spine in an automobile rider. The mechanism of fractures of the atlas is discussed, as well as embryonic development, the variations and abnormalities of this vertebra. The exceptional trend for decalcification and the lack of callus formation in this region deserve special consideration. As no re-examination could be performed, definite decision as to the nature of the lesion is postponed.

19 West Seventh St.

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EDITORIAL

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ROENTGEN KYMOGRAPHY

Interest in roentgen kymography has been gradually increasing since Dr. Pleikart Stumpf, of Munich, devised the multiple slit grid in 1928. At this stage in the development of kymography it seems appropriate to discuss the principles and purposes of the procedure and to emphasize its defects and shortcomings. Basically, kymography is a method for graphically recording the functional or physiological movements of an organ or structure on an x-ray film. Kymograms are records of movement. The procedure is limited by the following factors:

(1) Only organs or structures that are bordered by tissues of a contrasting density can be studied kymographically.

(2) Many organs and structures possess complicated movements in several different planes, such as the heart, which not only enlarges and contracts laterally and medially, but simultaneously changes its size in a vertical plane and also undergoes a rotary motion about a central axis. Unfortunately, a kymogram is but the record of one component of these complex motions.

(3) In recording the movements of a rounded or an obliquely placed object, the only motion accurately registered is that which occurs in a direction parallel to the slits and with the border of the object lying at right-angles to the slits.

(4) Only pathologic lesions that alter the way in which a structure moves, functions, fills, or empties, produce kymograms with characteristically different waves or records.

Keeping these limitations in mind, roentgen kymography is a reliable method for studying the motions of suitable structures and can be successfully used wherever it is desirable to record in detail the extent, direction, speed, duration, and time occurrence of movement. Kymography is not designed to replace roentgenoscopy, but to supplement it. The procedure may be considered as an additional and specialized tool to the armamentarium of the radiologist for the study of the physiologic motion exhibited by organs and structures. It is especially well adapted for research and investigative work in cases in which a permanent and objective record is required.

Clinically, the heart has been most extensively studied. The information obtained from kymograms has been useful in confirming established knowledge rather than introducing new ideas. Kymography has, however, served as a great impetus to the clinical study of cardiac physiology. It has added a physiologic aspect to the radiologic interpretations of heart disease. If this additional bit of knowledge aids in the diagnosis, then kymography is of value. In the diagnosis of the average cardiac patient in whom the history, physical examination, and laboratory reports are available, the roentgen kymogram will not provide additional information. It may be regarded as helpful, but not necessary, and somewhat comparable to the degree of importance given to the electrocardiogram. In selected cases the kymogram may be the main factor in establishing or confirming the diagnosis.

In the interpretation of kymograms the size and shape of the cardiac silhouette should be analyzed first. Then the movement waves are studied with the prospect of gaining additional information.

The respiratory movements of the ribs, diaphragm, lungs, and mediastinum can be easily recorded by kymography. The study of thoracic movements may become one of its chief uses. The stomach, duodenum, kidney pelvis, and ureters have been similarly studied, but kymograms of these organs are of less practical value because of their slow movements and the consequent long exposure time.

Mechanically the apparatus is simple and commercially perfected. Home-made equipment is satisfactory if the slits are accurately

spaced, of uniform width, and not wider than 0.5 mm. The film must move smoothly and at a uniform rate of speed. Small films (10 × 12) may be used for the heart, to lower the cost.

As with all new methods, familiarity with a procedure is gained through experience and practice. Confidence is established by confirming the diagnoses at the operating table and postmortem examination, but only time properly evaluates a procedure.

WENDELL G. SCOTT, M.D.

ANNOUNCEMENT

FIFTH INTERNATIONAL CONGRESS OF RADIOLOGY

PALMER HOUSE, CHICAGO

September 13–17, 1937

Membership in the Fifth International Congress of Radiology closed on Aug. 14, 1937. Early closing dates for membership in conventions of this character constitute one of the disappointing features which can not be avoided. Those who have forwarded their applications for membership since that date will understand that the officers and organizers of the Congress regret that it became necessary, inasmuch as the Portrait Catalogue and other publications of the Congress must be completed and ready for distribution when registration is opened at 1 P.M. Sunday, Sept. 12, 1937.

Attendance at the Congress is not limited to members of the Congress. By the payment of a small registration fee, one may be registered as a guest of the Congress and enjoy the full privileges of the scientific program and scientific exhibits throughout the period of the Congress.

Educational courses, which are free to members of the Congress, are open to registered guests of the Congress upon the payment of an additional registration fee. The very nature of the educational courses naturally limits the numbers that may be accommodated, and registration for the courses will close accordingly. For further information concerning these courses, please refer to the July issue of this Journal, page 119, or write your inquiry to the Secretariat, 2561 North Clark Street, Chicago.

The Grand Banquet, which occurs on Friday evening as the closing feature of the Congress, is free to all of the members and associate members.

Registered guests of the Congress will be required to purchase tickets at the registration desk if they wish to attend the Grand Banquet. They may also register associate members of the Congress by the payment of the regular associate membership fee.

It is exceedingly important that the guests as well as the associate members be registered as far ahead of the opening of the Congress as possible in order that the committees providing entertainment features may know the approximate number for which arrangements are to be made.

Contributions to the scientific program will be presented in the three official languages of the Congress. In addition to the language used by the essayist, the context of his address will be projected on a screen in the other two official languages of the Congress and they will be synchronized as far as possible with the address as it is delivered. It is obvious that this feature will add greatly to the success of this Congress, since a very great majority of the audience in the forenoon general sessions, and in the afternoon sectional meetings, will be English-speaking and -understanding, while the Contributors' presentations will be more equally divided between English, German, and French.

It would appear that almost every radiologist will endeavor to attend this Congress. It is the first opportunity American radiologists have had to attend a Congress within our own country with contributors representing all of the leading countries of the world. Furthermore, it is the first time that a program for an international congress of radiology has been so arranged that all of the guests will be able to understand any contribution they choose to hear.

With approximately 300 contributions on the program, one may choose papers from any phase of radiology and learn of the most recent advances in that particular field.

"Most of the European scientists are at least bilingual," explained Dr. Christie, President of the Congress, "but many United States physicians who will attend are not sufficiently conversant with more than English to comprehend many of the papers which will be read.

By translating every speech into English, French, and German, we believe that nearly everyone will receive the benefit of understanding the more than 250 speakers who will read scientific papers during the five-day meeting here September 13 to 17."

It will be the first International Congress ever held in the United States, Dr. Christie added, and will mark the forty-second year since Dr. William Conrad Roentgen discovered x-rays, and the thirty-ninth year since the Curies discovered radium. The vast progress made in development of the medical and other uses of these two boons to mankind will be portrayed during the Congress, not only through the scientific papers and discussions, but in actual graphic exhibits.

The Congress will be held at the Palmer House, Chicago, where more than 12,000 square feet of floor space will be devoted to an extensive scientific exhibit to be arranged by scores of hospitals and research laboratories throughout the world. Over 20,000 square feet will be devoted to commercial exhibits, showing the latest equipment manufactured by leaders in the field, ranging from x-ray negatives up to models of million-volt therapy apparatus.

A "short-term" medical school will be conducted during the Congress, said Dr. Christie. Eminent leaders in the field of radiology will conduct short courses during the Congress for the benefit of delegates who will attend the Congress from all parts of the world. All of the United States radiological societies, including the Radiological Society of North America, American Roentgen Ray Society, American College of Radiology, and American Radium Society, will hold their joint annual meetings during the Congress and will elect officers here. At least 500 foreign delegates are expected from 30 different countries, and over 2,000 United States physicians will attend.

Included among the outstanding scientists of the world who will be present at the meeting are: Dr. Gösta Forssell, of Stockholm, Sweden; Dr. Antoine Béclère, of Paris; Dr. Tamotsu Watanabe, of Osaka, Japan; Dr. H. Tellez-Plasencia, of Santander, Spain; Dr. Russell Reynolds, of London; Dr. William D. Coolidge, of Schenectady, N. Y.; Dr. C. Thurstan Holland, of Liverpool, England; Dr. George E. Pfahler, of Philadelphia, Pa.; Dr. Francis Carter Wood, of New York City; Dr. James Ewing, of New York City, and Dr. William J. Mayo, of Rochester, Minnesota.

COMMUNICATIONS

STANDARDIZATION COMMITTEE

December, 1936

I. Registry of Physicists.—Applications and examination results of 15 physicists were received by the Board and submitted to the Committee for approval. The following are certified as having met the requirements of the Board of Registry of X-ray Physicists (for previous certifications, see RADIOLOGY, May, 1936, **26,** 634):

M. M. D. Williams, Mayo Clinic, Rochester, Minnesota.
J. D. Leitch, Dept. of Health, Ontario, Canada
G. H. Henderson, Dalhousie University, Halifax, Nova Scotia.
E. L. Harrington, University of Saskatschewan, Saskatoon, Canada.
G. M. Shrum, University of British Columbia, Vancouver, Canada.
J. Demers, University of Montreal, Montreal, Canada.
M. M. Schwarzschild, Beth Israel Hospital, New York City.
J. E. Rose, Swedish Hospital, Seattle, Washington.
I. H. Blatz, Dept. of Hospitals, 414 E. 26th Street, New York City.
A. Omberg, 1273 Carr Avenue, Memphis, Tenn.
R. E. Pugh, 1944 Summit Avenue, Pasadena, Calif.
Irwin Vigness, University of Minnesota, Minneapolis, Minn.
L. Jacobson, Montefiore Hospital, New York City.
L. Rovner, Chicago, Ill.
M. C. Reinhard, State Institute for Study of Malignant Disease, Buffalo, New York.

The question was raised as to how sharp a line should be drawn between industrially employed physicists who are ineligible for certification and those physicists employed in strictly clinical, standardization, or consultative capacity. "Manufacturer," in the sense used by the Committee, means any person, group of persons, or company which is directly interested in the manufacture or sale of any article or equipment to the radiologist. The Committee desires, however, to place on record that it recognizes the high quality of the physicists employed by the various manufacturers and does not mean to imply in any sense

that they do not possess the same qualifications as a registered physicist. One of the principal purposes of the Registry is to establish a list of physicists available for consultative purposes without being hampered by any possible industrial affiliations.

It was agreed that any registered physicist who, subsequent to his certification, becomes affiliated with a manufacturer, shall automatically and without notice be dropped from the certified list. If such a physicist closes such an affiliation, a new application for certification may be submitted to the Board.

II. Certified X-ray Standardization Laboratories.—In the interests of radiology it is agreed by the Committee that all dosage meters in clinical use shall be calibrated and certified by a recognized x-ray standardization laboratory, meeting the following requirements:

1. Equipment must be in charge of a full-time physicist, whose special field is that of x-rays and whose basic training has been in physics.
2. The standardizing laboratory must be equipped with the necessary working standards for effecting a complete calibration of the current measuring system.
3. Standardizing equipment must be maintained in working order and position and not be disassembled except for purposes of normal maintenance.
4. Basic parts of the standardization equipment must be compared against that of the National Bureau of Standards (or the National Research Council of Canada, if in Canada).
5. Standardization equipment must be inspected *in situ* by a physicist selected by the N. B. S. or the N. R. C. C.
6. Standardization equipment must be in accord with "X-ray Standards and Units Standardizing Procedure of the National Laboratories" (Am. Jour. Roentgenol. and Rad. Ther., 1934, **31,** 815).
7. Laboratory must file with the N. B. S. drawings showing all essential details of ionization chamber, tube container, and diaphragm system. Any subsequent changes must be filed with the originals.

In this connection, it should be noted that the physicist in charge of such standardization laboratories need not necessarily be a Registered Physicist, but that in any case his general qualifications must meet at least as high a standard thereas.

The following laboratories have satisfied the necessary requirements under the above classification:

1. National Bureau of Standards, Washington, D. C.
   Physicists: Lauriston S. Taylor, George Singer.
2. National Research Council of Canada, Ottawa, Canada.
   Physicist: G. C. Laurence.
3. Cleveland Clinic, Cleveland, Ohio.
   Physicist: Otto Glasser.
4. Memorial Hospital, New York City.
   Physicists: G. Failla, Edith Quimby, Leo Marinelli.
5. Temple University, Philadelphia, Pa.
   Physicist: George Henny.
6. Victoreen Instrument Company, Cleveland, Ohio.
   Physicists: John A. Victoreen, Lawrence Frazer.

The above laboratories are certified to make calibrations for x-rays generated by potentials up to 200 kv. (peak). There are at date of writing, no laboratories certified to make calibrations for x-rays generated by potentials in excess of 200 kv. (peak). It is hoped that the National Bureau of Standards may be in such a position within a short time.

III. Sub-committee on Treatment Data Recording Charts (U. V. Portmann, Chairman, E. C. Ernst, Edith Quimby).—Final agreement was reached on a standard form for the recording of all treatment data. This will be published separately at an early date. With this will be published a full description of the entries with necessary details and precautions in making any measurements and calculations involved.

In addition, it is recommended that the radiologist in charge of an x-ray department maintain a day-book for recording all changes in tubes and apparatus, calibration changes, and calibration reports. It is suggested that all individual treatment records be initialed by technician and radiologist on such factors as filter, target-skin distance, and dose administered. This is particularly important for legal purposes.

In connection with the calibration of clinical x-ray installations, the importance of the field size used for the measurements was stressed. Particularly in the case of oil-immersed tubes and super-voltage tubes, it is

found that the dosage rate tends to increase with increase in field size. This is due principally to scattering from the large volume of oil. A sub-committee under Dr. Otto Glasser was appointed to prepare a report on this and related questions.

IV. Sub-committee on Units, Definitions, and Nomenclature (R. R. Newell, Chairman).—A full report was deferred until the next meeting of the Committee. In the meantime, it was suggested that the Journal's Publication Committee refer any questions relating to units to Dr. Newell, who is representative of the Radiological Society on the Radiological Units Committee of the A.I.E.E.

V. Sub-committee on Diagnostic Standardization.—A detailed report was prepared by Dr. G. Henny, Chairman, but action relating thereto was deferred until the next meeting, before which time members may have a better opportunity to study his report.

VI. Measurement of Super-voltage X-rays and Gamma Rays.—The Committee feels that adequate measuring standards for super-voltage x-rays and gamma rays are non-existent at this time. Work by Jaeger, Mayneord, Friedrich, Failla, Gray, and others is recognized as having great importance but not yet carried to the point where definite standards may be safely established. It seems evident that free air measurements will be impracticable for gamma rays.

Choice of the type of standard ionization chamber for super-voltage x-rays should be very definitely left open for the present. Thimble chambers can undoubtedly be used for clinical purposes, although the ultimate correct design is open to question. Work by Glasser and by Victoreen up to 400 kv. appears to contradict other equally reliable measurements of the so-called "saturation wall thickness." Four or five mm. of bakelite or carbon wall thickness may be unnecessary and actually undesirable at lower voltages. They do not find strong evidence for the flat-topped wall-thickness curve. Hence, at least for super-voltages up to 400 kv., we may reasonably question some of the similar earlier work.

Open air ionization chamber measurements have been made up to 800 kv. Mayneord showed a definite divergence at about 250 kv., but this was due to use of too small a parallel plate chamber. Up to the point where his chamber size became the limitation, his measurements showed good agreement between open air and thimble ionization. Lauritsen and Jaeger have shown that under suitable laboratory conditions free air chambers may be used for accurate measurements of super-voltage x-rays. Hence, we feel that *thimble chamber standards should not be adopted for x-rays until all the possibilities of free air measurements have been adequately explored.*

VII. Filters for X-ray Treatments.—The following approximate filter combinations are recommended by x-ray treatment work:

Copper + 1 mm. Al;
Tin + 0.25 mm. Cu + 1 mm. Al;
Lead + 1 mm. Sn + 0.25 mm. Cu + 1 mm. Al.

For the last two, it is desirable to have such a combination as to effectively cut off all wave lengths longer than 0.1 Å. In this connection, it is important to stop the passage of large amounts of radiation near the absorption limits of the particular filters used. Further details will be given in Dr. Glasser's later report.

VIII. Quality.—For clinical purposes, a statement of the fore-filter and half value layer gives an adequate quality description (fore-filter includes inherent filtration of tube and container). Use of a second half value layer is unwarranted. For fundamental and more accurate quality descriptions, the full absorption curve (or data) may be given. Only through the latter may other different quality measurements be related.

Quality measurements up to 400 kv. shall be made with copper. It is recognized that while tin is more discriminating, the difference from copper is not important. Moreover, it is desirable to keep down the number of filter materials. Tin, in pure and uniform sheets, is not easily handled and its use may involve uncertain errors if special precautions are not taken. Lead absorption data are probably desirable above 400 kv. but here again copper may possibly be sufficient for practical purposes.

The manufacturers shall be asked to give a statement with each x-ray tube or the inclosure of the exact copper equivalence of the walls, and the voltage for which this applies. On permanent apparatus this may be marked on the apparatus itself.

IX. Miscellaneous.—It is suggested that the manufacturers provide "pre-reading" voltmeters with more open scales and more reliable calibration than is frequently done. Since the technician relies upon this meter so much

for control purposes, it is essential that the instrument be reliable and readable.

Registered physicists, calibrating an x-ray plant, should see that all protection requirements are met, and report any omission to the radiologist in charge. A copy of such a report should be retained.

It is suggested that radiologists or hospitals installing new apparatus choose in advance the physicist who will do the subsequent calibration work. Advance consultation on apparatus, protection, and dosage measurement may be of great assistance to the radiologist and help to avoid expensive later changes.

Attention should be directed to the accurate timing of dosage. Errors in clock controls may be very considerable for short exposures of high dosage rate. The question of timers is being studied by Dr. Weatherwax and Dr. Chamberlain.

It was suggested that advance copies of this report be sent to members of the International Committee on Radiological Units and others interested.

LAWISTON S. TAYLOR, *Chairman*

ADVISORY BOARD FOR MEDICAL SPECIALTIES

The annual meeting of the Advisory Board for Medical Specialties, which is the co-ordinating Board of the twelve certifying boards in the various specialties, the Association of Medical Colleges, the American Hospital Association, the Federation of State Medical Boards of the U. S. A., and the National Board of Medical Examiners was held at Atlantic City, N. J., on June 6, 1937.

The following officers and members of the Executive Committee were elected:

Willard C. Rappleye, M.D., *President*, New York City; W. P. Wherry, M.D., *Vice-president*, Omaha, Neb.; Paul Titus, M.D., *Secretary-Treasurer*, Pittsburgh, Pa.; W. B. Lancaster, M.D., Boston, Mass., and R. C. Buerki, M.D., Madison, Wis., members of the Executive Committee.

Dr. Louis B. Wilson, of Rochester, Minnesota, the retiring president of the Board, was elected an emeritus member of the Board.

TAXING PROVISIONS OF THE SOCIAL SECURITY ACT

Delinquent employers of persons working in private x-ray laboratories were advised to-day by Commissioner of Internal Revenue Guy T. Helvering to make immediate tax returns as required under the provisions of Titles VIII and IX of the Social Security Act to avoid further payment of drastic penalties which are now accruing.

Commissioner Helvering pointed out that every person working in private x-ray laboratories came under the provisions of Title VIII, which imposes an income tax on the wages of every taxable individual and an excise tax on the pay roll of every employer of one or more. This tax is payable monthly at the office of the Collector of Internal Revenue. The present rate for employer and employee alike is 1 per cent of the taxable wages paid and received.

Under Title IX of the Act, employers of eight or more persons must pay an excise tax on their annual pay roll. This tax went into effect on January 1, 1936, and tax payments were due from the employers, and the employers alone, at the office of the Collector of Internal Revenue on the first of this year. This tax is payable annually, although the employer may elect to pay it in regular quarterly installments.

The employer is held responsible for the collection of his employee's tax under Title VIII, the Commissioner explained, and is required to collect it when the wages are paid the employee, whether it be weekly or semi-monthly. Once the employer makes the 1 per cent deduction from the employee's pay, he becomes the custodian of Federal funds and must account for them to the Bureau of Internal Revenue.

This is done, Mr. Helvering said, when the employer makes out Treasury form SS-1, which, accompanied by the employee-employer tax, is filed during the month directly following the month in which the taxes were collected. All tax payments must be made at the office of the Collector of Internal Revenue in the district in which the employer's place of business is located.

Penalties for delinquencies are levied against the employer, not the employee, the Commissioner pointed out, and range from 5 per cent to 25 per cent of the tax due, depending on the period of delinquency. Criminal action may be taken against those who willfully refuse to pay their taxes.

The employers of one or more are also required to file Treasury forms SS-2 and SS-2a. Both are informational forms and must be filed at Collectors' offices not later than next July 31, covering the first six months of the year. After that they are to be filed at regular quarterly intervals. Form SS-2 will show all the taxable wages paid to all employees and SS-2a the taxable wages paid each employee.

Participation in a State unemployment compensation fund, approved by the Social Security Board, does not exempt employers from the excise tax under Title IX, Commissioner Helvering said. Nor does the fact that there is no State unemployment compensation fund relieve the employer of his Federal tax payments. In those States where an unemployment compensation fund has been approved, deductions up to 90 per cent of the Federal tax are allowed the employer who has already paid his State tax. These deductions are not allowed unless the State tax has been paid.

This tax is due in full from all employers in States having no approved fund. The rate for 1936 was 1 per cent of the total annual pay roll containing eight or more employees, and for 1937 it is 2 per cent. The rate increases to 3 per cent in 1938 when it reaches its maximum. The annual returns are made on Treasury form 940.

An employer who employs eight or more persons on each of twenty calendar days during a calendar year, each day being in a different calendar week, is liable to the tax. The same persons do not have to be employed during that period, nor do the hours of employment have to be the same.

Actual money, when paid as wages, is not the sole basis on which the tax is levied. Goods, clothing, lodging, if a part of compensation for services, are wages and a fair and reasonable value must be arrived at and become subject to the tax.

Commissions on sales, bonuses, and premiums on insurance are wages and taxable.

Officers of corporations, whether or not receiving compensation, are considered employees for the purpose of taxation.

Wages paid during sick leave or vacation, or at dismissal, are taxable.

Travelling expenses required by salesmen are not wages if the salesmen account for, by receipts or otherwise, their reasonable expenditures. That part for which no accounting is made is construed as a wage and is taxable.

Exercise great care in filling out Treasury forms SS-1 and 940. Directions are easy to follow and correct returns mean no unnecessary delay.

IN MEMORIAM

With profound sorrow The American Board of Radiology records the untimely passing of a distinguished fellow-member, Doctor Willis F. Manges, November 24, 1936.

Renowned as physician and radiologist, Doctor Manges logically was appointed to the Board at its inception. As a member of this body he served the interests of his chosen specialty with extraordinary fidelity and efficiency. Outstanding among his traits were his deep sincerity, absolute fairness, unimpeachable integrity, and remarkably sound judgment. Because he was wise, we looked to him for safe counsel; because he was eminently fair, we relied on him to make certain that no injustice was wrought by any act of ours; because he was steadfast, we counted confidently on his unfailing friendship. So long as we shall live his memory will abide with us, and through the years to come radiology and radiologists will reap the benefit of his unselfish work in their behalf.

It is ordered that this declaration be spread on the minutes, that it be published in the radiologic journals, and that the Secretary of the Board transmit a copy to Mrs. Manges with assurance of our heartfelt sympathy and respect.

A. C. Christie, *President.*
B. R. Kirklin, *Secretary.*

June 3, 1937.

BOOK REVIEWS

Reports of the Second International Congress of Social and Scientific Campaign Against Cancer, Brussels, Belgium, Sept. 20–26, 1936, under the patronage of His Majesty the King and Her Majesty Queen Elizabeth. Volume I, General Reports, published under the direction of Mm. le Docteur Marta Fraenkel. A volume of

503 pages. Published by Ligue Nationale Belge contre le cancer, Brussels, 1936.

This is a series of reports by specialists, each outstanding in his particular field, on the modern views of the etiology, diagnosis, treatment, and prevention of various types of malignant tumors. Each paper is reproduced in full in the language of the author and summarized in German, English, Spanish, French, Italian, and Russian. The table of contents of the volume is as follows:

(*A*) *Scientific Cancerology*

I. *Biology.*

1. Carcinogenic agents:
Cook, J. W., Haslewood, G. A. D., Hewett, C. L., Hieger, I., Kennaway, E. L., and Mayneord, W. V. (London): Chemical Compounds as Carcinogenic Agents (report in English) 1
Borst, M. (Munich): Organic Substances of Growth (German) 24
Murphy, J. (New York): Inhibition of Malignant Growth by a Factor from Normal Tissue (English) 43
Gye, W. E. (London): Tumors Transmissible with Viruses 48
Pentimalli, F. (Florence): Transmissible Carcinogenic Agents (report in Italian) 59
Roffo, A. H. (Buenos Aires): Physico-chemical Etiology of Cancer (report in Spanish) 71
Vles, F. (Strasburg), and de Coulon, A. (Lausanne): Study of Various Physical and Physico-chemical Carcinogenic Factors (report in French) 88

2. Factors of predisposition and of resistance to carcinogenesis:
Kreyberg, L. (Oslo): Genetic Factors in the Development of Spontaneous and Induced Tumors in Animals (report in English) 115
Lynch, C. (New York): Present Aspects of Cancer in Relation to Heredity (report in English) 122
Fischer-Wasels, B. (Frankfort-on-Main): General Predisposition to Cancer (report in German) 133
Reding, R. (Brussels): Predisposition and Resistance to Cancer (report in French) 159
Teutschlaender, O. (Mannheim): Humoral Regulations and Tumoral Formations (report in German) 205

II. *Diagnosis.*

1. Progress in histological diagnosis and prognosis:
Ewing, J. (New York): Problems in Histological Tumor Diagnosis (report in English) 215

2. Progress in serological and serocytological diagnosis:
Hirszfeld, L. (Warsaw): On the Scientific Bases of the Serodiagnosis of Cancer (report in German) 227
Del Rio Hortega, P., and Ibanez, R. (Madrid): Recent Research Work on Serological and Serocytological Diagnosis of Cancer (report in Spanish) 240
Rondoni, P. (Milan): Critical Study on Recent Experiments on Serological and Serocytological Diagnosis of Cancer (report in Italian) 262

III. *Therapeutics.*

1. Progress in surgical treatment:
Hartmann, H. (Paris): Progress in Surgery in the Treatment of Cancer (report in French) 277
Petroff, N. (Leningrad): Recent Progress in the Surgical Treatment of Rectum Cancers (report in Russian) 292
Dogliotti, A. (Modena): Treatment of Pains from Tumors (report in Italian) 309

2. Progress in radiotherapy:
Wood, Francis Carter (New York): Progress in X-ray Therapy (report in English) 320
Schinz, H. R. (Zurich): Progress in X-ray Therapy (report in German) 331
Mallet, L. (Paris): Tele-x-ray-therapy of cancers (report in French) 334
Holthusen, H. (Hamburg): X-ray Radiobiology (report in German) 352

3. Progress in medical treatment:
Auler, H. (Berlin): Chemotherapy of Malignant Tumors: Its Physico-chemical Bases (report in German) 361

Blumenthal, F. (Belgrade): Organotherapy of Cancer (report in German) 379
Maisin, J., and Pourbaix, Y. (Louvain): Organoprophylaxy (report in French) 389
Freund, E. (Vienna): Diets and Cancer Treatment (report in German) 407

(*B*) *Social Campaign against Cancer*

I. *Access of patients to diagnosis and treatment.*
Athias, M. (Lisbon): General Organization of the Anti-cancer Campaign (report in French) 419
Lerat, P. (Brussels): Social Principles of the Campaign against Cancer (report in French) 427
Sand, R. (Brussels): Social Medicine and Anti-cancer Campaign (report in French) 430

II. *Medico-social assistance to the incurables.*
Le Bret, R. (Paris): Medico-social Assistance to the Incurables (report in French) 435

III. *Cancer and demography.*
1. Statistics of morbidity and mortality of cancer:
Cramer, W. (London): The Importance of Statistical Investigations in the Campaign against Cancer (report in English) 441
Dormanns (Munich): Comparative Statistics on Geographical Distribution of Cancer in the Reich over the Period 1925 to 1933 (report in German) 460
Dublin, L. (New York): Statistics on Morbidity and Mortality from Cancer in the United States (report in English) 483
2. Cancer and races:
Bonne, C. (Batavia): Cancer and Human Races (report in English) 492

TRAITE DE CHIRURGIE ORTHOPEDIQUE. By L. OMBREDANNE, Professeur de clinique chirurgicale infantile et orthopedie à la Faculté de medecine de Paris, membre de l'Academie de medecine, chirurgien de l'hôpital des Enfants-malades, and P. MATHIEU, Professeur de clinique de chirurgie orthopedique de l'adulte à la Faculté de medecine de Paris, chirurgien de l'hôpital Cochin. Volume III. Published by Masson et Cie., Paris, France, 1937. Price, for five volumes complete, 1250 fr.

The third volume of this System of Orthopedic Surgery seems to me to be by far the best of the three volumes thus far reviewed and has set a high standard for such a work.

After a chapter on tumors of the spine which covers those lesions in a comprehensive manner the remainder of the volume is taken up with a discussion concerning the upper extremity. Starting with the scapula and going down to the hand and fingers, each anatomical part is treated separately but a complete discussion of the various lesions affecting those parts is given. All are excellently illustrated and fully covered, with little in the way of superfluous discussion. Much of these chapters concerns fractures and their complications and sequelæ. This seems reasonable, as the importance of fractures of the arm and particularly those around the elbow cannot be over-estimated.

Adequate discussion is given to the congenital lesions such as elevation of the scapula, club hand, Madelung's deformity, etc. The work will serve as a most excellent reference book for those seeking information on any of these subjects.

One of the most complete and best presented reviews of the subject of injuries of the carpus that I have ever seen is found here. The common inflammatory lesions are covered adequately, too, and treatment as well as diagnosis and prognosis is well outlined.

Several types of treatment of these various lesions are presented. Many are unfamiliar to the reviewer but look worthy of application.

The volume is excellently illustrated by photographs, roentgenograms, and by drawings as necessary. Beautifully printed, it has, along with the other volumes, set a high standard in that respect. The material and its arrangement in this volume seems to us most excellently conceived and, as we have already said, it has set a high mark for others to reach.

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L. G. JACOBS, M.D., of Madison, Wis.
E. T. LEDDY, M.D., of Rochester, Minn.
DAVIS H. PARDOLL, M.D., of Chicago, Ill.
ERNST A. POHLE, M.D., Ph.D., of Madison, Wis.
WILLIAM R. STECHER, M.D., of Easton, Pa.
CHARLES G. SUTHERLAND, M.B. (Tor.), of Rochester, Minn.
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ANIMAL EXPERIMENTATION

Roentgen Therapeutic Experiments in Erythroleukotic Chicken. E. Forfota. Strahlentherapie, 1937, **58,** 295.

Leukemia in chicken occurs in two different types, one contagious and one non-contagious type. The lymphadenosis cannot be transferred to other animals and this is the most frequent type. The myelosis, however, and especially the erythroleukosis, can be transferred from animal to animal. The author used finely mashed liver of a chicken which had died from the disease dissolved in 10 per cent physiological sodium chloride solution and injected from 0.5 to 1 c.c. intravenously in healthy chickens. Seventeen out of 18 developed the disease. He then studied the effect of roentgen rays on its course. Technic: 150 kv., 50 cm. F.S.D., total body exposure with from 80 to 180 r, with aluminum and copper filtration; exposures were given on the sixth and ninth day or every second day. The course of the disease was uninfluenced in the irradiated animals. The virulence of the contagion was also the same whether taken from untreated controls or treated chicken. This was checked through to the fifth generation. It appears, therefore, that the erythroleukosis in chicken is far more resistant than leukemic diseases in man.

ERNST A. POHLE, M.D., Ph.D.

Changes in the Spinal Fluid in Animals Following Short Wave Therapy to the Brain. R. Glauner and E. Schorre. Strahlentherapie, 1937, **58,** 286.

The authors applied a six-meter wave to the head of rabbits by means of Schliephake electrodes of 4 cm. diameter at 1 cm. distance. The single application lasted 30 minutes and a total of 10, 15, and 20 sittings were given. Following this therapy, definite chemical changes were found in the spinal fluid. The proteins and the sugar content were increased. These changes were maintained for a long period of time up to 30 weeks. There seems to be a relation between the dose and the effect.

ERNST A. POHLE, M.D., Ph.D.

THE BLADDER

Diverticulum of the Urinary Bladder. Neil S. Moore. Southern Med. Jour., March, 1937, **30,** 263–267.

From an evaluation of this brief analysis, it is apparent that the author held the following conclusions: In addition to the indisputable theory of congenital tendency to urinary diverticulosis, the exciting causative factors are contracted bladder necks and hypertrophy of the prostate. Statistics of individual physicians may vary according to the type of work done. The diagnosis is comparatively simple if routine cystoscopic and cystographic examinations are made. Small buds, single or multiple, will probably remain stationary if the obstructing lesion is removed by transurethral methods. If, however, the bladder is opened by suprapubic incision, it is advisable to remove all pockets at the same time.

Large diverticula should certainly be removed. The most satisfactory method is complete external excision working through the opened bladder with a finger inserted into the collapsed sac as a guide. Spinal anesthesia in moderate sized doses, seldom exceeding 100 mg. of procaine hydrochloride, has been of material benefit in allowing complete relaxation and ample exposure of the operative field. In careful hands and with average good fortune spinal anesthesia is the safest of all anesthetic agents in bladder surgery. Ample drainage of the bladder and all dependent pockets will reduce morbidity and mortality.

A rather extensive bibliography accompanies the article.

DAVIS H. PARDOLL, M.D.

Management of Atonic Bladder Due to Obstruction of Vesical Neck. Louis M. Orr, II. Southern Med. Jour., May, 1937, **30,** 519–524.

While in recent years much has appeared in the literature on cord bladder, there has been a paucity of information on this particular subject as viewed by the writer.

Regardless of the type of method employed in eliminating the obstruction, atonicity may persist due to a loss of elasticity in the vesical musculature. The author advocates partial resection of this inelastic area in order to correct the loss of tone and to relieve the retention of urine.

A case presentation, cystograms, and discussion accompany this interesting article.

DAVIS H. PARDOLL, M.D.

BONE DISEASES (DIAGNOSIS)

Sunray Hemangioma of Bone. William E. Anspach. Jour. Am. Med. Assn., Feb. 20, 1937, **108,** 617–620.

Only 21 cases of hemangioma involving the skull have been found in the literature. Of 1,831 neoplasms of bone recorded at the bone registry, 13 have been hemangiomas. Three of these involved the skull. Earlier reports failed to distinguish hemangioma from sarcoma, the "sunburst" appearance on roentgenograms apparently largely responsible for the error in interpretation.

The tendency for hemangioma of bone to produce a somewhat characteristic picture on roentgenograms seems to be due in part to the type of bone involved. It should be considered in all "sunburst" tumors of bone, but a malignant neoplasm should be considered equally probable when there is a sunray pattern on roentgenograms of long bones, especially if there has been active destruction of bone. Sharply defined, well organized trabeculæ or spicules favor hemangioma.

Hemangioma of flat bones produces a beautiful sunray

formation on roentgenograms. Hemangioma of long bones often produces a "loose soap bubble" appearance but almost as frequently the sunray pattern of density. When hemangioma involves vertebræ, a vertical striated appearance is produced which is almost characteristic of this one type of tumor.

CHARLES G. SUTHERLAND, M.B. (Tor.).

THE BREAST (BENIGN)

Roentgen Therapy of Puerperal Mastitis. R. Goedel. Strahlentherapie, 1937, **58,** 651.

The author has used the following technic in the treatment of puerperal mastitis: 170 kv., 3 ma., 30 cm. F.S.D., 0.5 mm. Cu, 50 r surface dose, to be repeated on three or four successive days. The best results were seen if the treatment was started within 12 hours after the symptoms appeared. Twenty-nine out of 30 cases of acute mastitis, or 97 per cent, healed without incision following radiation therapy.

ERNST A. POHLE, M.D., Ph.D.

CANCER (DIAGNOSIS)

Experience with the Klein Reaction. G. Hepp. München. med. Wchnschr., Aug. 21, 1936, **83,** 1378–1380.

In an open series of cases, there was a percentage of 93.4 correct diagnoses, as contrasted with 90.2 per cent confirmation in the unknown series. The test does not differentiate carcinoma from sarcoma. Excellent results were obtained in differentiating prostatic hypertrophy from prostatic carcinoma, and mastopathia chronica cystica from mammary carcinoma.

WILLIAM R. STECHER, M.D.

Experiences with the Klein Cancer Reaction. C. Reimers. München. med. Wchnschr., Aug. 21, 1936, **83,** 1375–1377.

In the writer's experience with the Klein reaction for the detection of malignancy over a period of two years, he has found it correct in 90 per cent of his cases, when positive; and even higher when malignancy was not present.

WILLIAM R. STECHER, M.D.

Experience with the Carcinoma Demonstration Serologic Test of Lehmann-Facius. H. Reploh and H. Middledorf. München. med. Wchnschr., Aug. 21, 1936, **83,** 1380, 1381.

In their series of 350 cases, in which 100 presented clinical signs of carcinoma or sarcoma, the Lehmann-Facius reaction gave 94 per cent positive results, and 4.2 per cent unspecific results.

WILLIAM R. STECHER, M.D.

Experience with the Klein Test. Fritz Grögler. München. med. Wchnschr., Aug. 21, 1936, **83,** 1377, 1378.

In 90 cases in which the Klein test was employed, in which malignancy was suspected, 92.6 per cent showed a positive reaction which was confirmed clinically later.

WILLIAM R. STECHER, M.D.

CANCER (THERAPY)

Contact Therapy. Strahlentherapie, 1937, **58,** 606–623.

Six authors contributed to a discussion of contact therapy, *i.e.*, the treatment by means of an x-ray tube which can be introduced into the body cavity and brought into contact with the lesion.

W. Schaefer (p. 606) has used it in the treatment of carcinoma of the cervix. An observation period of from six months to three years, of 88 patients, shows that the results so far have been encouraging. The statistical evaluation still suffers from the fact that the number of patients treated is relatively small.

W. Weibel (p. 609) gives also the preliminary results obtained at the Women's Clinic of the University of Vienna with the use of contact irradiation in carcinoma of the female generative organs. His total material comprises 56 cases which includes 38 patients with inoperable carcinoma of the cervix. The immediate results up to an observation period of one year were very satisfactory.

H. Chaoul (p. 611) reports excellent results obtained in the treatment of carcinoma of the skin and the lip, and also in malignant melanomas. Quite satisfactory response was also seen in carcinoma of the oral cavity, glandular organs, and carcinoma of the rectum, and in sarcoma. The patients have been under observation from one to five years, and out of a total of 307 cases, 76 per cent were free from symptoms at the time of the report. Forty-five patients were treated more than three years ago, and 14 of those more than four, and three of those more than five years ago.

F. Melchart (p. 614) believes that the future development of contact therapy will be along the lines of further approach to radium. The economic side is, of course, of great importance since roentgen therapy with the contact method is less expensive than radium treatment.

A. Frank (p. 618) has used the method for a year and a half and reports a few illustrative cases. In addition to malignant tumors, he also treated two patients with hemangioma of the buccal mucosa; their lesions reduced in size after the application of 6,000 r. He feels that the contact method can be used successfully in many cases which otherwise would have to be treated by radium.

P. Merio (p. 623) has treated 12 cases with malignant neoplasms with contact therapy, applying doses of from 6,000 to 12,800 r. The temporary results in five cases were good.

ERNST A. POHLE, M.D., Ph.D.

The Co-operation of Surgeon and Radiologist in the Treatment of Tumors of the Upper Respiratory and

Digestive Tracts Considered from the Roentgenological Viewpoint. E. G. Mayer. Strahlentherapie, 1937, **58,** 636.

In many instances operative procedures facilitate adequate irradiation of malignant tumors. The author mentions the advantage of tracheotomy and resection of the thyroid cartilage in the treatment of carcinoma of the larynx, gastrostomy in irradiation of the stomach, and provision of adequate drainage in carcinoma of the sinuses before radiation therapy.

ERNST A. POHLE, M.D., Ph.D.

Histologic Changes in Cutaneous Cancer Following Irradiation. Paolo Trerotoli. Archivio di Radiologia, 1936, **12,** Nos. 3–4, 221–243.

The author studied histologically some sections taken from cutaneous ulcerated carcinomas at various intervals following treatment with various doses and qualities of radiation. The histologic picture is variable, with the exception of the eosinophiles, which are more numerous when the reaction is more severe, and of the fat droplets, which seem to be independent of time and the number of irradiations.

E. T. LEDDY, M.D.

Methods of Radiation Therapy of Cancer with Extremely High Potentials. A. Gunsett. Strahlentherapie, 1937, **58,** 573.

The author describes his 800 kv. generator used in the treatment of cancer and gives data regarding output and the effect of potential, filter, and field size on the depth dose, amount of back-scatter, and the skin reactions to be expected. The increase in the depth dose amounts to 30 per cent if the tube potential is increased (from 200 to 520 kv.). The amount of back-scatter is definitely reduced; it is possible, therefore, to apply larger doses to the skin. The field of usefulness for these extremely hard rays is perhaps limited to deep-seated malignancies.

One interesting observation concerns the changes in the blood picture when comparing 200 and 520 kv. radiation. Patients treated with the shorter rays showed a higher absolute drop in leukocytes and also a rather striking increase of the sedimentation velocity of the erythrocytes. The author is optimistic regarding the future of high voltage therapy. He believes that within a relatively short time the cost of this type of apparatus will become low enough so that its general use will be possible.

ERNST A. POHLE, M.D., Ph.D.

Fractional and Protracted Fractional Radiation Therapy: Experiences at Zurich. H. R. Schinz. Strahlentherapie, 1937, **58,** 373.

The author relates his experience with the fractional method in the treatment of malignant tumors based on an analysis of 800 cases seen during the period 1919–1935. He believes that irradiation of malignant neoplasms is local treatment. The tumor must receive a lethal dose; the effect of irradiation is direct both upon the cancer cell as well as on the blood vessels in the tumor. It is important to utilize the elective effect of irradiation, *i.e.*, use the difference in sensitivity between cancer tissue and normal tissue to radiation. The total dose should be applied in as short a time as feasible rather than to give several series at long intervals. A number of illustrative cases are discussed with detailed data regarding dosage. The methods used are simple fractionation and protracted fractionation with high intensities and simple fractionation and protracted fractionation with very small intensities.

In a series of tables the results obtained in the treatment of the various tumors are evaluated statistically. There is no question but that the Coutard method using protracted fractionation with a small number of r per minute brings about clinical cures which are impossible with other methods of application. Radium implantation or electrocoagulation are used in this connection only to remove small residual masses or small recurrences. The author believes that with this method of treatment his results are as good as those obtained in other institutions having available large quantities of radium.

ERNST A. POHLE, M.D., Ph.D.

THE COLON

Roentgenographic Studies of the Mucous Membrane of the Colon. III.—Mucosal Detail Studies as an Aid in the Early Recognition of Carcinoma of the Colon. Henry G. Jacobi and Franz J. Lust. Am. Jour. Med. Sci., April, 1937, **193,** 510–515.

The use of "mucosal detail" study of the colon for small and early organic lesions has been neglected in this country, though the method has been used abroad with apparent success. The authors present their method of study of the mucous membrane of the colon which has proved satisfactory in their patients. The procedure is as follows: "The first essential for the proper execution of this method is to have as clean a colon as is possible. To effect this the preparation of the patient begins a day previous to the actual examination, during which time only a slight low-residue diet is allowed. In the evening before the examination a dose of milk of magnesia or cascara is given. The following morning two enemas, containing about a quart of water with some Castile soap, are used at one-hour intervals. From two to three hours after the last enema, the patient is ready for examination. A cup of tea or coffee may be allowed in the morning but nothing else. The barium enema itself consists of about one quart of barium mixture prepared in plain water. No milk or mucilage is to be used in the preparation of this solution as such tends to delay the evacuation of the colon.

"The slow administration of the barium enema is then started under proper fluoroscopic control, in order to detect the presence of stenosing lesions immediately. As soon as the tip of the contrast material has reached

the hepatic flexure of the colon it is discontinued. The patient is then instructed to turn on his right side. Very often the barium will fill out the cecum without giving more barium. Too much contrast material, if administered, will not only cause distress but in many cases results in leakage into the small intestine. When this has occurred, the subsequent evacuation of the large bowel upon which the success of this method depends will be seriously hindered and will make proper mucosal study almost impossible. A film is then taken with the patient lying on his abdomen. The patient is then instructed to evacuate as much of the barium enema as possible. Repeated fluoroscopic examination is then made to determine whether the correct amount of barium is present to outline the mucosal wall. Sometimes the period of evacuation may take from 30 to 45 minutes. Naturally, no technician can be entrusted with this procedure."

Three cases are reported in which the "mucosal detail" method proved of service in making an early diagnosis of an organic lesion of the colon which had previously been unobserved by the routine barium enema. The authors feel that with the early diagnosis of colon malignancy by such a method one can expect better therapeutic results than obtained in the past.

G. E. Burch, M.D.

COUTARD METHOD

Roentgen Injuries of the Parotid Gland. H. H. Hermann. Strahlentherapie, 1937, **58,** 220.

The parotid gland of a patient with carcinoma of the pharynx showed histologically lipomatosis and loss of the glandular structure following irradiation according to the Coutard method. In order to determine the causal relation between the roentgen exposure and the histologic change the author irradiated the parotid glands of 11 rabbits (180 kv., 0.5 mm. Cu + 1.0 mm. Al, 40 cm. F.S.D.). Doses of from 1,600 to 5,000 r were applied; five animals were treated over one parotid at one sitting, two with the fractional dose method and two with the Coutard method—the same as the patient. The microscopic studies of the glands indicated that irradiation was not responsible for the lipomatosis. The acute reaction within the gland, swelling, dry mouth, and edema of the face is temporary. Little difference was noted between the reactions in glands treated with simple fractionation and according to Coutard. Injury to the parotid glands seemed to be more likely with the protracted fractional dose method. From an economical standpoint, simple fractionation is undoubtedly preferable.

Ernst A. Pohle, M.D., Ph.D.

THE CRANIUM

Auxiliary Methods in the Diagnosis of Space-occupying Intracranial Diseases. Hugo Krayenbühl. Schweiz. med. Wchnschr., Jan. 30, 1937, **65,** 89–94.

The author mentions as necessary supplements to clinical examination, roentgen study of the skull, ventriculography and encephalography, exploratory ventricular puncture, and cerebral angiography.

Roentgen study of the skull may show abnormal calcification, displacement of normally calcified pineal gland, choroid plexus, or falx, or of air shadows. Especially important are changes in the skull bones known to be associated with tumors.

Ventriculography and encephalography have the great advantage that practically every space-occupying lesion produces a displacement of the ventricular system. The type of lesion cannot in general be ascertained from a ventriculogram. It shows only changes from normal in form and size of the ventricles. Encephalography is indicated in cases without clinical evidence of risk of brain stem herniation, usually focal and general epilepsy, as well as certain cases of chronic hydrocephalus.

Exploratory ventricular puncture is indicated in cases in which one wishes to verify the neurologic diagnosis; it is the method of choice in cases of coma, and in cases in which the pressure changes preclude ventriculography. While the interpretation is beset with pitfalls, it may make possible a life-saving operation.

Cerebral angiography is especially valuable in vascular intracranial lesions, as aneurysms, and in the diagnosis of tumors by the changes they produce in the vascular bed. Displacement of vessels may be observed.

Illustrative cases, some good drawings, and some fair reproductions of roentgenograms are included.

L. G. Jacobs, M.D.

ENDOCRINE GLANDS

The Relation of the Endocrine System to Malignancy. Charles L. Martin. Am. Jour. Roentgenol. and Rad. Ther., September, 1936, **36,** 314–321.

The secretions from certain organs in the body, especially the spleen, thymus, thyroid, and adrenal glands, seem to exert an antagonistic effect on the growth of malignant tumors. The secretions from the ovary seem to favor the growth of benign tumors in the uterus and breast and malignant tumors in the breast.

No effective gland extracts for the eradication of cancer have as yet been prepared, but the withdrawal of the ovarian hormone by castration produces marked benefit in certain advanced cases of cancer of the breast, especially those with bone metastases. Pain is often relieved and bone metastases improved by new bone replacement. Cases are cited.

S. M. Atkins, M.D.

THE EYE

Effect on the Eye of Radium Used for Treatment of Malignant Disease in the Neighborhood. Philippa Martin. British Med. Jour., March 27, 1937, 651–654.

The author, observing the changes produced in the

eyes when radium was used in their vicinity, undertook to study the radium injuries to the eyes.

Radium, when employed near the eyes in treating malignancies, damaged the conjunctiva, iris, cornea, and lens. The conjunctival irritation is manifested early by congestion, edema, and a serous discharge or a mucopurulent discharge at times. Pain is not frequent even in a severe conjunctival reaction. Some of the late conjunctival effects are scarring, adhesion to the globe and lids, and ectropion.

The iris may be affected and the involvement evidenced by pain, slight swelling of the iris, and posterior synechia.

The chief manifestation of damage to the cornea is ulceration. This may result from the direct action of irradiation or may result indirectly as from dryness of the cornea caused by reduced lachrymal activity from irradiation. Exposure of the cornea when the lids are kept open by chemosis resulting from the conjunctivitis may also cause ulceration. Diminution in sensation in the cornea is one of the earliest signs of damage. Later there is a loss of the normal corneal luster. The ulcers may progress to perforation with the resulting complications.

Radium cataract is another late reaction to irradiation, and appears two years or more after exposure. This probably arises from interference with the nutrition of the lens caused by endarteritis and telangiectatic changes in the ciliary body.

The author discusses the causes of such ocular complications in irradiation therapy to malignancies in the vicinity of the eyes, and also presents the methods for avoiding or minimizing such undesirable results.

G. E. Burch, M.D.

THE FIBULA

A Rare Luxation: Isolated Luxation of the Fibular Head Anteriorly. G. Imhäuser. München. med. Wchnschr., Aug. 21, 1936, **83,** 1383, 1384.

It is not unusual to have associated luxation of the fibular head with a fracture of the fibula, but a luxation *per se* is very rare. The literature is reviewed, and an additional case is proffered. Roentgenographically, the diagnosis is simple in a typical case.

William R. Stecher, M.D.

FOREIGN BODIES

Osseous Bridging of Vertebral Bodies Resultant of a Foreign-body Abscess. Ulrich. München. med. Wchnschr., Dec. 11, 1936, **83,** 2049, 2050.

A brief but excellent review of the two main types presenting osseous bridging of the vertebral bodies is presented and differential diagnostic roentgenologic features are stressed. These types are namely, Bechterew's disease and spondylo-arthrosis deformans.

The author presents another etiologic factor causing somewhat analogous signs which are secondary to irritative reaction of a pre-vertebral abscess, due to lodging of a metallic foreign body. This is rather rare, for commonly such a circumstance produces pressure atrophy of vertebral bodies due to transmitted pulsation of the aorta. The main reason that a diagnosis of Bechterew's disease was not made was the restriction of the osseous bridging to the site of the abscess.

William R. Stecher, M.D.

GALL BLADDER (NORMAL AND PATHOLOGIC)

Cholecystographic Findings Following Cholecystostomy. E. L. Jenkinson and Joseph M. Foley. Am. Jour. Roentgenol. and Rad. Ther., September, 1936, **36,** 301–304.

Cholecystostomy does not necessarily leave a pathologic gall bladder behind as previous authors concluded, for of 28 patients who had had their gall bladders surgically drained from eight months to many years before, 19, or 68 per cent, showed a normal functioning with the dye (Keaphen B) examination.

S. M. Atkins, M.D.

GASTRO-INTESTINAL TRACT (DIAGNOSIS)

Duodenal Diverticula. Walther Thaler. München. med. Wchnschr., Dec. 11, 1936, **50,** 2055–2058.

Duodenal diverticula may be symptomless or present symptoms if marked stasis of food occurs, with ensuing diverticulitis, hemorrhage, abscess formation, gangrene, and perforation. The lack of muscularis and peristalsis in the diverticulum predisposes to retention, particularly in the presence of a narrow neck. The presence of a diverticulitis by direct extension is productive of gastritis, duodenitis pancreatitis and cholangitis, cholecystitis, and hepatitis. In addition, pressure symptoms on neighboring organs by a filled diverticulum may be the only symptoms. The incidence as shown roentgenologically is from 1.2 to 1.7 per cent but anatomically 3 to 13 per cent is found. In the author's series of 1,100 gastro-intestinal examinations, 1.5 per cent showed duodenal diverticula. The most common site is the descending portion of the duodenum, particularly in the vicinity of the papilla of Vater, and almost always in the concavity of the duodenal loop. The size varied from that of a lentil to a small apple, and oddly in this series a predominance of females presented diverticula, with occasional double diverticula. Clinical symptoms are vague but summed up as follows: (1) Symptoms are improved in certain postures and by massage; (2) symptom of dullness are almost constant and of long standing; (3) gaseous gastric eructations, nausea, loss of appetite, flatulence, constipation, and loss of weight are common findings. However, in any non-typical gastric disturbance a roentgenologic examination is indicated, and these are readily noted if a careful examination in horizontal and vertical positions, with exposures in many planes, are obtained. Roentgenologic criteria are, briefly: (1) A well-defined density with

sharply circumscribed contour, in the confines of the duodenum; (2) a portion of the barium passes over, or beside, the suspicious density, showing the site of the neck of the diverticulum; (3) the contrast fleck remains after emptying of the duodenal loop; (4) hours to days, occasionally show retention of barium in the diverticulum; (5) absence of tenderness, when no diverticulitis is present, suggests a diverticulum rather than an ulcer niche; (6) in compression technic, the mucous membrane pattern is visualized in contradistinction to an ulcer crater loss of outline.

Treatment is mainly conservative, and along the lines of peptic ulcer. If ineffective, surgical removal is then considered.

WILLIAM R. STECHER, M.D.

Polypoid Tumors of the Duodenum and Small Intestine. Ferdinando Talia and Pasquale Ficara. Archivio di Radiologia, 1936, **12,** Nos. 3–4, 190–220.

Talia and Ficara first discuss the incidence of polypoid gastro-intestinal tumors which are commonest in the rectosigmoid and rarest in the stomach and upper intestine. The symptomatology and clinical findings permit the holding of only a tentative diagnosis of polyp. It is only by roentgenologic examination that diagnosis can be made with precision. Some characteristic cases are illustrated. The authors favor surgical treatment of polyps because of the possibility of malignancy in them. The paper is accompanied by a good bibliography.

E. T. LEDDY, M.D.

GYNECOLOGY AND OBSTETRICS

Is It Possible to Injure the Genes in the Reproductive Organ of Women by Radium and Roentgen Rays? C. Weysser. Strahlentherapie, 1937, **58,** 470.

The relation between irradiation by roentgen rays or radium of the female pelvis and injury to the future offspring is still a matter of debate. The author reports two illustrative cases belonging to this group. One woman, 32 years of age, was treated over the abdomen for actinomycosis. The right ovary was in the beam and the left ovary could not be entirely protected. Roentgen rays were applied according to the Coutard method with a total dose of 2,300 r. Three months after the treatment the patient was cured. Five months later she became pregnant and delivered a normal child weighing 3 kg. The second patient had been treated by intra-uterine radium screens because of tuberculosis of the uterus (1,200 mg.-hr., 50 mg. in 1 mm. Al for 24 hours). The ovaries were, of course, included in the irradiated area. However, the woman became pregnant again six months later. The child was born six weeks after term and was dead at birth. The delivery was difficult because of stenosis of the cervical canal. The fetus appeared normal and weighed 3,450 grams.

The author does not believe that there is a direct connection between irradiation and death of the child. Whether the abnormal length of the pregnancy was due to the radium treatment is impossible to state. He concludes that in his opinion there has been no proof offered yet that roentgen and radium irradiation of women in the child-bearing period will injure the genes.

ERNST A. POHLE, M.D., Ph.D.

The Diagnosis of Tubal Pregnancy. Albert Mathieu. Jour. Am. Med. Assn., Jan. 30, 1937, **108,** 366–369.

There is probably no more dramatic incident in the life of a physician than that of the text-book type of ruptured tubal pregnancy. Those cases with the typical history represent only a small percentage. The others, not typical, are at times very difficult to diagnose. The diagnosis cannot be made unless the physician has the condition in mind. He must remember that any vaginal bleeding in the child-bearing age, following a missed period, may possibly mean an ectopic pregnancy. Discussion is limited almost entirely to the diagnosis and among the more or less unusual diagnostic methods the author reports practically 100 per cent correct diagnoses from hysterosalpingography in the several cases in which it was used. The abortion of the tubes was beautifully visualized, and he was able to establish what seems to be a pathognomonic x-ray sign for a tubal pregnancy in the midportion of the tube. In cases of tubal pregnancy aborting from the distal end of the tube, the injected oil entered all the crevices between the aborting pregnancy and the walls of the distal ends of the tubes in such a way that it literally draped itself about the mass and allowed this oil-covered mass to be visualized by the x-rays. The injection into the uterus and tubes of iodized oil in a case of tubal pregnancy he considered practically harmless.

CHARLES G. SUTHERLAND, M.B. (Tor.).

HEART AND VASCULAR SYSTEM

Situs Inversus of the Abdominal Organs with Congenital Heart Failure and Right Aortic Arch. H. Grieshaber. Schweiz. med. Wchnschr., Dec. 26, 1936, **52,** 1307, 1308,

The author presents an excellently studied case of situs inversus of the abdominal organs, with persistent right aortic arch, and ventricular septal defect with incomplete rotation of the heart. The one significant roentgenologic sign for future diagnostic aid is the fact that the author proves that the position of the diaphragm is not resultant of pressure displacement of the liver but rather to the position of the heart. Thus, in primary cases of dextrocardia, the left diaphragmatic cupola is on a plane with the right. Pathognomonic signs of right aortic arch are given, namely, absence of aortic knob and pulsation to the left, indentation of the esophagus along the dorsum, and the fact that the triangle to left of the superior aspect of the tracheal bifurcation is missing. Excellent clinical discussion relevant to differentiation of the various types of congenital cardiac malformations is appended.

WILLIAM R. STECHER, M.D.

INFLAMMATORY DISEASES

The Method of Irradiation with Small Doses. W. Wieser. Strahlentherapie, 1937, **58,** 646.

The author briefly discusses the principles of radiation therapy in inflammatory disease. In acute cases the doses varied between 15 and 100 r effective in the diseased tissue; chronic inflammations receive from 1 to 100 r per sitting. Some examples are given to illustrate the necessity of individualization and the danger of cumulative effect in cases of prolonged treatment.

ERNST A. POHLE, M.D., Ph.D.

THE KIDNEYS

Congenital Polycystic Disease of the Kidneys. Hugh R. Spencer. Southern Med. Jour., May, 1937, **30,** 524–527.

The author summarizes polycystic disease of the kidneys as follows: It is a congenital affection characterized by the formation of multiple cysts in both kidneys and in the liver in 30 per cent of the cases.

The incidence is about 1:3523 hospital admissions and 1 in every 500 autopsies. There is no difference in sex incidence. The disease is seen in the newborn and in adults in or past the third decade.

The disease results from embryologic maldevelopment.

Symptoms are directly or indirectly the result of a progressive pressure atrophy of renal parenchyma or of infection.

The important clinical findings are: mass, urinary changes characteristic of renal failure, decreased phthalein output, a well tolerated non-protein nitrogen retention, intermittent hematuria, and hypertension.

The characteristic findings on pyelography are:

(*a*) Elongation of the pelves and major calices, with blunting of the minor calices.
(*b*) Right angulation of the ureter in its relation to the pelvis.
(*c*) Displacement of the ureter toward the midline.
(*d*) Bilateral pelvic changes.

DAVIS H. PARDOLL, M.D.

KYMOGRAPHY

Roentgen Kymographic Observations on the Behavior of the Heart in Hot Baths. Joseph Ritter. München. med. Wchnschr., Feb. 26, 1937, **84,** 339–341.

The author considers that, although the action of hot baths on the circulatory system is little understood and although their use is on an empirical basis, they have a certain place in stages of decompensated heart disease. He sought to study the heart changes in hot baths with a roentgen kymograph of the multiple slit type, arranged over the tub so that the patient need not be moved. After mention of the methods of previous observers and their errors, it is pointed out that the method (of size observation) has intrinsic errors, and that tendencies to enlargement may be within the limits of experimental error. For this reason functional observations are important. The author's observations show that a hot bath can produce an extraordinary increase in heart action, as measured by stroke volume; in addition, there is increased filling and pulsation of the great veins; an increase of the vascular lung markings, and decreased apical beat. He also believes this method of study opens the way to a better understanding of the various factors, such as temperature of the bath, water pressure, effervescence, and so on.

L. G. JACOBS, M.D.

Roentgenologic Demonstration of Swallowing Function Disability. Max Dahm. München. med. Wchnschr., Dec. 11, 1936, **83,** 2050, 2051.

An interesting demonstration of how kymography enables one to delineate minimal degrees of swallowing dysfunction, employing a barium meal, is discussed. Ordinary technic in many instances would not disclose the disordered function, particularly the type of paralytic origin, *viz.*, multiple sclerosis, bulbar paralysis, pseudo-bulbar paralysis, post-encephalitis. A detailed account of the various actions of the component parts in swallowing, together with altered activity in paralysis, is given.

WILLIAM R. STECHER, M.D.

THE LUNGS

Fleeting Pulmonary Infiltration with Eosinophilia. W. Loffler. Schweiz. med. Wchnschr., Nov. 7, 1936, **45,** 1069–1076.

Fifty-one observed cases showing this benign syndrome are reviewed, portraying the discrepancy between the alarming objective signs and benignity of the course of the syndrome. The roentgenograms show patchy soft-appearing infiltration, which superficially strongly resembles an advanced pneumonitis. Surprisingly, in a few days there is disappearance of the pulmonic signs and concomitant absence of eosinophilia, which is quite marked in the case of pulmonic infiltration. Roentgenographically, the characteristics of this entity are the inordinately rapid localization and disappearance of the pulmonary infiltration, which varies from flaky to cloudy structure, either demarcated or fading out in the periphery, and single or multiple, or unilateral or bilateral. The entire metamorphosis occurs in from three to eight days. This fact shows the importance of serial roentgenographic re-check, for the greatest confusion lies in mistaking this for a tuberculous process.

The eosinophilia may reach 66 per cent with a leukocytosis of 14,000 and an absolute count of 9,000 is not unusual, as contrasted to a norm of 320. The eosinophilia is always present in this entity and usually maxi-

mal just after the height of the pulmonary infiltration, but the author emphasizes the fact that this is not a simple post-infectious eosinophilia. There is no analogy between the size of infiltrate and degree of associated eosinophilia.

The symptom-complex can be summated as: (1) Roentgen pulmonic shadow, which is fugacious, with a concomitant eosinophilia; (2) extremely slight or no definable subjective symptoms; (3) occasionally slight elevation in temperature, and uncommonly an irritative cough.

Ascaride larvæ were never found in the sputum, for this was strongly suspected in presence of marked eosinophilia. The lesion could be confused roentgenologically with the terminal pneumonic stage, just before resolution, but rarely is there such an associated eosinophilia in this affection.

General types of pulmonic infiltration can be classified as : (1) Large irregular shadows, unilateral or bilateral; (2) round focus type resembling the Assmann early pulmonary tuberculosis type; (3) multiple pluricentric unilateral or bilateral infiltrate; (4) infiltration sharply demarcated to one pulmonic lobe; (5) type resembling secondary infiltration of pulmonary tuberculosis, and only distinguished by eosinophilia.

In most cases careful examination reveals a fine pleuritic friction rub; and roentgenologically, thickened pleura may be localized, particularly to the interlobar fissure. There is a definite seasonal frequency to the syndrome, namely, maximum in July and August. Two-thirds of the cases were in males. The main etiologic considerations were helminthic infestations and an anaphylactic process. The former has many advocates for it is known that the *Ascaride* larvæ temporarily sojourn in the lung structure. The opinion that the phenomenon is a reaction to a pollen is not met with favor by the author. Other possibilities entertained are bronchial asthma and partial pulmonic atelectasis. Of greatest importance is the differential diagnosis of tuberculosis but rarely does tuberculosis produce such a degree of eosinophilia, though occasional findings of from 4 to 7 per cent have been recorded. Another differential factor is the absence of termination into necrosis or evidence of fibrotic replacement in this symptom-complex.

The tuberculin reaction was negative in one-third of the cases, in spite of the fact that no children were in the group tested. If tuberculosis is considered as the etiology, then it is of a hitherto unknown benign form. The author regularly re-examines the chest over a long period of time to eliminate a possible recrudescence and exhibition of tuberculosis. The present conception of this symptom-complex is that it is a microbide of the lung but possibly could be a tuberculide.

WILLIAM R. STECHER, M.D.

Artificial Pneumonia and its Treatment. C. Fried. Strahlentherapie, 1937, **58,** 430.

The beneficial effect of roentgen rays in the treatment of inflammatory disease is well known; this includes also diseases of the respiratory tract. Some investigators have reported good results in the treatment of pneumonia and this induced the author to study the mechanism of the effect experimentally. Six guinea-pigs were injected in the trachea with from 0.3 to 0.5 c.c. of *Staphylococcus aureus hemolyticus* suspension. Three animals were irradiated and three served as controls. Treatment consisted of from 90 to 95 r (in air) applied once (160 kv., 0.5 mm. Cu + 1 mm. Al, 30 cm. F.S.D.). A total of 60 animals were treated in this manner and killed at varying intervals. The macroscopic and microscopic examinations of the irradiated lungs showed that there was less infiltration, less hyperemia, less edema, congestion, and exudate than in the untreated controls. From the microscopic studies it appeared that following early irradiation the inflammatory process does not fully develop; if irradiation is done later, for instance after 24 hours, the fully developed pneumonia takes a less severe course.

ERNST A. POHLE, M.D., Ph.D.

The Roentgenologic Picture of Gangrenous Suppurative Lesions of the Lung. Giuseppe Pilotti. Arch. di Radiol., 1936, **12,** Nos. 3–4, 153–176.

Pilotti illustrates some selected cases of pulmonary gangrene, points out the characteristics of the suppurative process, and emphasizes the value x-ray examination may have, not only in establishing a diagnosis but also in furnishing valuable indications for treatment. The differential diagnosis of the various types of suppuration is discussed in detail.

E. T. LEDDY, M.D.

Congenital Lung Cyst. J. Cash King and L. C. Harris. Jour. Am. Med. Assn., Jan. 23, 1937, **108,** 274–279.

Congenital cyst of the lung may be defined as an intrapulmonary fluid sac of which the wall is composed of bronchial tissue and the fluid content is a product of the bronchial epithelium. Its formation is attributed to an anomalous occlusion of the bronchus in the embryo. In the last decade 152 cases have been described. The growth may be masked by secondary complications, such as abscess or rupture, and may be overlooked by the pathologist unless the bronchi are carefully searched for the site of obstruction. Those cases not diagnosed clinically which undergo spontaneous recovery never come to autopsy. Therefore, the number of cases found at autopsy gives an inaccurate conception of its true incidence. The condition is now being recognized with increasing frequency with present-day improved methods of roentgenologic technic.

It is almost unanimously agreed that cystic disease is congenital in origin. In 1928 Mueller published an excellent article giving a critical review of theories advanced prior to that time, to which the reader is referred.

All fluid cysts of the lung are caused by Jackson's so-called stop-valve occlusion. When the wall of the cyst is sufficiently strong to support an intracystic pressure

which inhibits the secretory activity of the mucous cells of the germinative lining membrane, the fluid cyst remains as an asymptomatic parasite. Infection of a cyst may occur by extension of bacteria through its walls, causing isolated abscesses. If the cyst ruptures into the pleural cavity, a hydrothorax results; or if infected, a pyothorax results. If pneumatized tissue is encountered in rupture, air will be present above the fluid line.

Any classification which goes beyond the division of congenital and acquired constitutes merely an enumeration of the different pathologic states that may develop in the progress of the growth.

Unfortunately, there is no symptom or train of symptoms pathognomonic of lung cysts. Many cases without secondary infection are symptom-free and may not be recognized at all.

In their review of the literature, the authors found only one instance in which a clinical diagnosis of uncomplicated lung cyst was made prior to roentgenologic examination.

An analysis of the reported cases indicated a high mortality rate in infants and children. Fluid cysts do not of themselves carry a grave outlook, but the development of infection and the establishment of bronchial communication are fatal complications.

CHARLES G. SUTHERLAND, M.B. (Tor.).

Roentgen Therapy in Primary Carcinoma of the Lung during 1928–1936. L. Popovic. Strahlentherapie, 1937, **58,** 543.

The paper consists mostly of a tabulated analysis of the cases of carcinoma of the lung observed by the author. They are grouped according to the type of treatment given. Five patients received incomplete therapy, nine were treated according to the fractional method, 48 with the saturation method, and eight with the Coutard method. A small percentage of the patients were temporarily improved.

ERNST A. POHLE, M.D., Ph.D.

The Rôle of Atelectasis in Post-operative Pulmonary Complications. Editorial. Jour. Am. Med. Assn., March 13, 1937, **108,** 887, 888.

Post-operative pulmonary complications occur in from 2 to 4 per cent of all operative interventions. When operations on the upper abdominal region alone are considered, this figure rises to 10 per cent and higher. The mortality from the same cause is given as 0.6, or one in every 200 cases. Studies revealed that the introduction of local and spinal anesthesia did not diminish either the morbidity or the mortality from this cause.

Research on the pathogenesis of the post-operative pulmonary complications resulted in three distinct theories: that of aspiration pneumonitis, that of infected emboli, and, more recently, that of pulmonary atelectasis.

Since William Pasteur, in 1910, revived interest in post-operative collapse of the lung, the number of reported cases has risen, so that Coryllos believed its incidence to be nearer 50 or 75 per cent.

The most striking clinical and roentgenologic sign of massive collapse of the lung is the unusually high position and immobility of the diaphragm. A reduction of the vital capacity to 30 and 50 per cent of the normal in patients following an abdominal operation has been demonstrated. There is a direct relationship between the reduction in the vital capacity and the incidence of pulmonary complications.

The second factor is the accumulation of mucus in one or another bronchus. The air in the occluded lung or lobe is absorbed and collapse of the alveoli follows.

The two important factors in determining the collapse are the viscid and tenacious mucus in the bronchial tree and the impairment of the natural means of defense, namely, coughing, respiratory movements, and ciliary action.

The more or less temporary occlusion of a bronchus leads to the absorption of the alveolar gases of the collapsed lung. The further course of the atelectasis will depend on the duration of the obstruction and the virulence of micro-organisms contained in the mucous exudate causing the obstruction. The presence of virulent pneumococci will cause pneumonia; the presence of pyogenic organisms may lead to suppuration, and the presence of certain fusiform anærobes to gangrene of the lung. Thus atelectasis, either patchy, involving small areas, or massive, is the forerunner of post-operative pneumonia or brochopneumonia.

CHARLES G. SUTHERLAND, M.B. (Tor).

LYMPHOGRANULOMA

Total Teleroentgen Therapy. F. Sluys. Strahlentherapie, 1937, **58,** 599.

For total body exposure to roentgen rays the author uses distances of from 2 to 2.5 meters and a filter of 0.5 mm. Cu + 2 mm. Al. The doses applied should not exceed 50 r, since, for instance, in Hodgkin's disease, even 15 r are poorly tolerated. The results were good in lymphatic and myelogenous leukemia; occasionally a patient with Vaquez' disease responded. A few cases with Hodgkin's disease were benefited, although no definite rules can be established as to the use of general body exposure in lymphogranulomatosis.

ERNST A. POHLE, M.D., Ph.D.

OSTEOMYELITIS

Acute Hematogenous Osteomyelitis in Children. Vernon L. Hart. Jour. Am. Med. Assn., Feb. 13, 1937, **108,** 524–528.

Acute hematogenous osteomyelitis is a local manifestation of a blood stream infection which is usually transient. The skeletal infection is always secondary to a remote infection, the source of which is usually the integument or the mucous membranes of the upper respiratory organs. A bacteremia necessarily precedes the localization of infection in the osseous system. Cultures of blood and pus demonstrate that the most common infective agent is *Staphylococcus aureus. Staphylococcus albus, Streptococcus albus, Streptococcus*

pyogenes and pneumococcus organisms are also frequent causative agents.

The first skeletal manifestation of the disease is constantly localized in a single metaphysis of one of the long bones of the extremities or in the juxta-epiphyseal region of other bones of the growing skeleton. The primary bone involvement is not in the medullary cavity or cortex of the main shaft of a growing bone. During the early acute stage of the disease the infection is limited to a single metaphysis. However, subsequent to direct or hematogenous spread of the infection and in the subacute or chronic phases of the disease the main shaft, the neighboring joint, and the medullary cavity may be affected. If the infection is not in the main shaft and medullary cavity during the acute stage there is no reason for their surgical exposure. The surgical attack should be limited to the site of infection or metaphysis.

The name "metaphysis" was first used by Kocher to describe the broad cancellous end of the diaphysis which is adjacent to the epiphyseal disk. The metaphysis represents the bone most recently developed from the epiphyseal cartilage or disk and is, therefore, more vascular, more delicate, more susceptible, and less immune than the older bone of the shaft, which is dense and compact. The marrow of the shaft, which occupies the medullary cavity, is "bountifully provided with cellular elements," while the marrow of the metaphysis, which fills the interstices between the trabeculæ of the cancellous bone, presents a "paucity of phagocyte cells."

The cortex of the middle of the shaft is either more or slightly less than one-fourth inch (0.64 cm.) in thickness, while the cortex surrounding the metaphysis is much thinner and near the epiphyseal disk it is paper-thin. This explains the ease with which infection within the cancellous metaphysis may perforate into the subperiosteal space and why the rupture is usually juxta-epiphyseal.

The metaphysis is richly supplied by the terminal branches of the nutrient artery. The vascularity of the juxta-epiphyseal region is abundant and consists of a bed of terminal capillary loops where the blood current is slowed and where infection is very likely to settle as a bacillary embolism.

The epiphyseal circulation is separated from the vascular system of the metaphysis by a practically avascular barrier, the epiphyseal disk.

The problem of joint involvement secondary to acute hematogenous osteomyelitis depends largely on the anatomic relationship between the joint capsule, the periosteum, the metaphysis, and the epiphyseal disk. Certain metaphyses are intracapsular (hip), while others are either entirely extracapsular (ankle) or intracapsular and extracapsular (shoulder). When a metaphysis is intracapsular the periosteum no longer protects the joint from involvement, since the greater portion of the periosteum is attached to and blends with the capsule instead of with the epiphyseal disk. Perforation of the intracapsular metaphyseal cortex and its thin periosteal covering permits the infection to invade the joint cavity directly. The metaphysis of the proximal end of the femur is completely intracapsular; infection of the hip joint is, therefore, the rule in acute hematogenous osteomyelitis of the proximal end of the femur. Perforation of the distal tibial metaphyseal cortex does not invade the ankle joint directly, since this metaphysis is entirely extracapsular. Clinical experience teaches that infection of the knee joint is an infrequent complication of acute hematogenous osteomyelitis of either the distal end of the femur or the proximal end of the tibia.

Surgical drainage of acute hematogenous osteomyelitis without joint infection should always be made through an extracapsular dissection.

CHARLES G. SUTHERLAND, M.B. (Tor.).

THE OVARIES

Contribution to the Irradiation of the Ovary. G. H. Schneider. Strahlentherapie, 1937, **58,** 238.

The author publishes a series of tables giving the doses required for temporary and permanent sterilization by roentgen rays, also for the treatment of uterine fibroids and cases with ovarian dysfunction. As an example it may be mentioned that he recommends for permanent sterilization in women from 20 to 25 years of age dosage of from 323 to 467 r, and for the age group from 46 to 50 years dosage of from 253 to 363 r effective in the ovary.

ERNST A. POHLE, M.D., Ph.D.

PEPTIC ULCER

The Frequency of Air under the Diaphragm in Perforated Gastric and Duodenal Ulcer. Sydney E. Johnson. Jour. Am. Med. Assn., Jan. 23, 1937, **108,** 295, 296.

Demonstration of spontaneous pneumoperitoneum is pathognomonic of perforation. The value of the sign depends on the percentage of cases in which the sign can be elicited. The charts of all patients admitted over a five-year period, with an admission diagnosis of perforated peptic ulcer, were studied. There were 76 cases, of which 30 had no x-ray examination. Thirty-five of the remaining 46 gave the positive finding of air under the diaphragm and 11 were negative.

Of the 11 negative cases, one was eliminated because it was found at operation that the ulcer had not perforated. Three others were excluded because there was no operative or necropsy confirmation of the clinical diagnosis. The remaining seven patients in the negative (x-ray) group were proved by operation to have perforated ulcers.

All of the 35 patients in the positive group were proved by operation to have perforated ulcers.

The time between the attacks and the roentgen examination in the 35 patients who showed air under the diaphragm ranged from one to 36 hours and averaged eight and one-half hours.

CHARLES G. SUTHERLAND, M.B. (Tor.).

PNEUMOTHORAX

A Case of Spontaneous Contralateral Pneumothorax and Artificial Pneumothorax. Jacques Stephanie. Schweiz. med. Wchnschr., Nov. 7, 1936, **45,** 1088, 1089.

A case of bilateral pulmonary tuberculosis with an artificial pneumothorax, left side, is presented, in which there was a sudden spontaneous pneumothorax of the right side.

WILLIAM R. STECHER, M.D.

RADIATION

Principles of X-ray Treatment. O. David. Schweiz. med. Wchnschr., Feb. 6, 1937, **67,** 120, 121.

The author points out that in spite of the older biologic units and the more recent physical unit, the "r," that the true therapeutic unit is the tolerance dose. This is known, from the works of several authors cited, to vary with the size and time relation of fractionation. He points out that in cases in which therapy is cauterizing, little individualization is possible. Special reference is had to cases in which limiting or stimulating vital processes are in question. It is pointed out that in thyrotoxicosis and lymphoblastoma therapy is essentially symptomatic rather than etiologic, and that for this reason the least amount that will control the symptoms is indicated; this *per se* rules out iron-clad schedules. Cumulative effects must be kept in mind. The author concludes with two axioms—that ill-guided therapy for the sick is worse than none, and that we ought forever to discard schematic therapy and keep to individualization, though more inconvenient and difficult.

L. G. JACOBS, M.D.

Principles of Radiation Therapy of Blastomatous and Hyperplastic Disease: The Single Massive Dose Method. H. Wintz. Strahlentherapie, 1937, **58,** 521.

The author has always advocated the application of the entire dose in as short a time as possible in roentgen therapy of malignant disease. In his clinic one series takes from four to five hours for carcinoma of the uterus; this is followed eight or nine weeks later by irradiation of the parametria. The patient usually is confined to the clinic for a period of only five or six days. Although this type of treatment requires most accurate dosage measurements, it is, in the author's opinion, most efficient in destroying the malignant growth. Some other advantages are that the total dose administered to the pelvis is relatively small as compared with the Coutard method; the difference in radiosensitivity between normal and diseased tissue is taken full advantage of, the skin is in good condition after the treatment, and no irreparable changes in the connective tissue within the pelvis have been observed. The economic factor is also in favor of this method, and the end-results in carcinoma of the uterus and of the breast have been excellent, according to his statistics.

ERNST A. POHLE, M.D., Ph.D.

RADIUM

Experimental Radium Poisoning. II.—Changes in the Teeth of Rabbits Produced by Oral Administration of Radium Sulphate. Maurice Rosenthal. Am. Jour. Med. Sci., April, 1937, **193,** 495–501.

The changes in the teeth of four rabbits were studied following the administration of 100 micrograms of radium sulphate. The teeth were studied at various intervals of time by photographic, autographic, and histologic methods.

Rosenthal found that the radium not only was stored in the alveolar bone but also in the teeth, producing definite changes in the morphologic picture of the tooth. The findings, as summarized by the author, showed that "there is a marked disturbance in calcification, with resorption of teeth and the formation of ankylosis by the ingrowth of newly formed bone, which also replaces the absorbed bone of the alveolar process. The essential changes in the enamel organ consist of flattening and atrophy of the ameloblasts, with hyperplasia of the stratum intermedium and subsequent degeneration and necrosis of the entire formative structure. The normal pulp tissue is replaced by abnormal, irregular secondary dentine masses. The surrounding periodontium shows an extreme hyperplasia of fibroblastic tissue, with invasion of surrounding structures. The development of cysts arising from epithelial rests in this membrane is also an interesting finding."

G. E. BURCH, M.D.

Radium Treatment with Small Intensities. K. Wasserburger. Strahlentherapie, 1937, **58,** 668.

The author has treated a number of lesions with radium applicators delivering small intensities. In thyrotoxicosis he uses from 40 to 50 mg. of radium filtered through 0.5 mm. Pt. This is left in place at 2 cm. distance for approximately 60 hours over a period of from 8 to 10 days. This corresponds to approximately 0.4 r/min. Eleven out of 14 patients became symptom-free. A similar technic was used in the treatment of plastic induration of the penis, in hemangioma, and in circulatory disturbances in the extremities. In some hemangiomas from 4 to 6 radium needles containing 2 mg. radium and filtered through 0.5 mm. Pt are inserted to apply about 40 per cent of the dose customary for a carcinoma of the same size.

ERNST A. POHLE, M.D., Ph.D.

SCLERODERMA

The Surgical Treatment of Scleroderma. Rene Leriche, Adolphe Jung, and Michael de Bakey. Surgery, January, 1937, **1,** 6–24.

Scleroderma is a term applied to the syndrome characterized by sclerosis, induration, and pigmentation of the skin, which may be localized or generalized, and frequently associated with asthenia, digestive disturbances, arthritis, muscle atrophy, and other symptoms depending on the gravity and degree of involvement.

The authors take up particularly the type in which a mild or atypical Reynaud's disease exists at or some time before the onset of the skin changes. They point out that locally there is a decreased vascularity of the skin with an increase in the tonicity of the arterioles and a diminished circulation. In addition, there is frequently an hyperparathyroidism with hypercalcemia and decalcification of the osseous framework.

Roentgenographic examination will occasionally show diffuse calcification which is not limited to the spongiosa but also involves the cortex. It is more pronounced in the extremities and is frequently localized in the hands and feet, especially the phalanges. Some cases were observed in which decalcification was so intense that the osseous structure of one or more phalanges was not distinguishable on the roentgenograms.

Treatment is concerned with perivascular sympathectomy to decrease the vasospasm or parathyroidectomy (or ligation of the inferior parathyroid arteries) to correct the endocrine dyscrasia. In cases with bilateral involvement both procedures were used. Results were satisfactory in most of the cases. The authors prefer the removal of the parathyroids.

JOHN E. WHITELEATHER, M.D.

THE SHOULDER JOINT

Backward Dislocation of the Shoulder. H. Wijnbladh. Nord. med. tidskr., Oct. 10, 1936, p. 1679. (Reprinted by permission from British Med. Jour., Dec. 12, 1936, p. 98 of Epitome of Current Medical Literature.)

The author has observed as many as seven cases of backward dislocation of the shoulder in a Swedish hospital between 1931 and 1935, and it seems that this dislocation is not as rare as the scanty space devoted to it in the textbooks would suggest. Of the two forms of this dislocation, the subacromial and the infraspinous, the former would seem to be the more common. The clinical picture of this dislocation was in all the author's cases characteristic, but its diagnosis was by no means easy in the muscular or fat cases. In the first case the correct diagnosis was not made before it was established by a radiological examination; and in a later case both the clinical and the radiological examinations were at first at fault, although the patient, a woman, was thin. The correct diagnosis was made next day when the radiological examination was repeated. In all seven cases reposition, with or without anesthesia, was easily effected simply by pulling on the arm in its long axis and exerting direct pressure on the head of the humerus from behind, or by direct pressure alone. But recurrence of the dislocation took place as easily as the reposition in two cases, and in one of these the shoulder had been put out of joint in the same way three times during the past two years. The duration of treatment ranged as widely as from one to twelve months, and in three cases troubles persisted in the form of pain at work and at night, loss of strength, and limitation of movement, notably that connected with abduction and outward and inward rotation.

THE SPINE

Anomalies and Fractures of the Vertebral Articular Processes. Wilbur Bailey. Jour. Am. Med. Assn., Jan. 23, 1937, **108,** 266–270.

Fissures across the vertebral articular processes may be formed by the presence of an ununited accessory center of ossification opposite the tips of the articular processes, or they may be the result of fracture of the articular processes. The differentiation between these can nearly always be made, if proper value is given to the history of the injury and to the appearance in the roentgenograms.

Fissures due to anomalies are usually transverse, well demarcated, and often bilateral or multiple.

Fractures of the articular processes in combination with severe injuries of the spine in which there is an actual dislocation of one vertebral body on another are not at all unusual. One or more articular processes are frequently sheared off under such circumstances. Isolated fractures in which the vertebral bodies alone are involved, however, constitute a rarity.

CHARLES G. SUTHERLAND, M.B. (Tor.).

THE STOMACH

Radiation Therapy of Inoperable Intra-abdominal Malignancy, with Special Reference to the Stomach. E. A. Merritt. Am. Jour. Roentgenol. and Rad. Ther., September, 1936, **36,** 324–331.

Radiation therapy of these lesions is advocated in that, of 13 cases treated since January, 1934, three are living and apparently well and free of all evidence of disease, as checked by roentgenological examination of their stomachs. One with roentgenologic evidence of disease is living. Nine are dead. These cases were taken without regard to condition of patient or extent of lesion.

Treatments were given daily except Sunday after the modified Coutard technic. One field over the anterior and one over the posterior stomach were employed with a total dose of about 2,500 r, voltage 200 kv.

S. M. ATKINS, M.D.

The Limits of the Possibilities of the Roentgen Diagnosis of Gastric Carcinoma. G. Hammer. München. med. Wchnschr., Dec. 11, 1936, **50,** 2035–2037.

The technical phase of the study of the stomach has been greatly advanced by the innovation of the recent procedures of mucous membrane relief pattern studies, kinematography of peristaltic waves, multiple superimposed projections, and the recently advocated kymographic method. In addition, the great advance in speed and sharpness of detail by the newer apparatus has greatly enhanced the detection of filling defects and disturbance in function and morphology of the stomach. Nonetheless, the important factors of cognizance of what is occurring in neighboring organs are not discernible, *viz.*, presence of metastasis in abdominal lymph nodes, or early metastatic nodules in liver, etc. The

author wishes to take inventory of our current expensive methods of diagnosis in gastric carcinoma.

It is a *sine qua non* that any hope of cure in gastric malignancy is entirely dependent upon early arrival at diagnosis, for in the light of present knowledge, surgical procedures should be effective. It is patent that in the vast majority of cases the patient will present himself for examination only when symptoms are present, which factor will in the majority of instances permit of diagnosis of a great percentage of far advanced malignancies. In contradistinction, there are many subjects who, having symptoms referable to the gastric tract, present themselves to the radiologist with unquestioning confidence that the examination will be conclusive in either demonstrating or eliminating a possible lesion. This immediately places the radiologist in the position of arbiter in the court of last appeal, and naturally the question arises, Is this justifiable? Can one attain such exactitude as is awaited by the referring physician? Berg is quoted as stating that in the face of negative findings roentgenologically one cannot be absolutely certain that malignancy is not present, for his experience proved that a small malignancy with widespread metastasis can be present, without altering the functional and morphologic outline of the stomach, and even the mucous membrane relief was not altered. In addition, roentgenologically undiagnosable, is malignancy infiltrating diffusely sub-mucously, with no fibrotic reaction.

The next issue is the question of diagnosis of malignancy without symptomatology, which diagnosis is the only tenable hope for cure. Finding of coincident beginning carcinoma of the stomach is not rare in autopsies with cause of death entirely unrelated. The number of such fortunate diagnoses roentgenologically is ridiculously small, suggesting that it has been overlooked in many instances. It is obvious that all malignancies commence cellularly and originally are microscopic in size, which fact precludes the diagnosis in this stage by any known methods. The question then resolves itself: Is an anatomico-macroscopic discernible carcinoma, which has caused changes in the gastric lining, always demonstrable roentgenologically? Inasmuch as there is no anatomic negative roentgenographic control, this question can be answered only by the experience of practice.

The common practice of reporting "negative" is strongly deprecated; for such an unqualified negation can be made only in the light of innumerable exposures obtained in numerous projections, etc. To wit, the rather high incidence of failing to diagnose a carcinoma of the cardia, which should be readily discerned by the deflection of the esophageal stream at the esophageocardiac juncture. In the author's experience not one case of thoroughly studied gastric series, which eventually went to operation or autopsy, showed the presence of malignancy, with the roentgen findings reported as negative. In many cases in which the primary tumor was not readily found but attributed to the stomach on account of the site of metastatic involvement, etc., the primary neoplasms were finally discovered in the gall bladder, biliary passages, pancreas, duodenum, and colon. The author emphatically states that it is not the method of examination, *i.e.*, whether the compression technic, or other refinement is employed, but the examiner who is at fault when an erroneous diagnosis is made. He also warns, not to excuse one's shortcomings by blaming the non-cooperation of the patient.

It is possible that the earliest diagnostic criteria will be those obtained by the kymographic method, showing dysfunction of peristalsis; but to date this has certainly not justified its claims. One must also consider the fact that an original "negative" gastric examination carries no weight later; for a carcinoma might evolve at a later date, which was not present at the time of original examination. Nonetheless, one can state with a great degree of security that a properly conducted negative gastric x-ray examination is of great weight.

Further difficulties in the presence of aberrations in the normal function and contour of the stomach present themselves in the differentiation of carcinoma from other entities, such as ulcer, syphilis, tuberculosis, amyloidosis, lymphogranuloma, etc. Of greatest practical importance is the differential diagnosis of benign ulcer and gastric malignancy. Though the main sign is the niche, rarely a carcinoma presents a similar finding, and in fact there may be malignant change in an ulcer. Haudek's description of ulcer niche and carcinoma crater is very reliable. Occasionally the differentiation is impossible even with laboratory findings and clinical studies; and most strangely may be confused histo-pathologically if biopsy or section is not obtained at just the correct site. The most common site for malignant change in an ulcer is in the prepyloric region near the angularis; never adjacent to the duodenum, and rarely in the ascending portion of the stomach. It behooves one, therefore, to consider any long-standing ulcer in the prepyloric region as potentially malignant—or rather, as undergoing malignant change—and to recommend operation. Only in this manner will the lesion be detected early.

Polyps, particularly solitary, may confuse one with early malignancy, but in general can be diagnosed radiographically. Again, the warning of the strong probability of malignant change in polyps makes it mandatory to have operative intervention for confirmation and removal.

The distinguishing signs between linitis plastica and circular antral carcinoma are not always absolute, and operative measures should be instituted when in doubt. In pyloric stenosis it is almost impossible to distinguish benignancy from malignancy, and again operation should be mandated.

Rare diseases such as syphilis, tuberculosis, amyloidosis, deformity due to adhesions, and extra-gastric tumors are sometimes difficult to diagnose. Gastric spasm, particularly of the pylorus, may not infrequently suggest an organic stricture, particularly in hypertrophic pyloric sphincter entity. The mucous

membrane pattern is of great help in distinguishing an infiltrating lesion from the above.

At times, marked hyperplastic gastritis will superficially resemble carcinomatous filling defect while additional suggestion of anemia, hematemesis, and loss of weight, with palpable resistance, add further difficulties. It is not uncommon to find localized hyperplasia in the antral region, and polyps are prone to develop therein. The opinion has been expressed that this latter entity should be considered as pre-cancerous and surgically removed.

Difficult simulants to distinguish are isolated lymphogranulomatous lesion of the stomach, leukemic and pseudo-leukemic infiltration of the stomach. In all questionable cases a therapeutic test of irradiation followed by shortly spaced intervals with re-examination will suggest a radiosensitive lymphoblastoma, if present. From a purely anatomical consideration, the lesions are radiographically indistinguishable from one another. A differential point between actinomycosis and carcinoma of the stomach is the predilection for the greater curvature in the former, but this is an unreliable criterion. Gastric sarcoma is rare and the site of predilection is along the greater curvature aspect near the fundus, often assuming a ball shape and indenting the diaphragmatic cupola.

One should not get the impression that gastric carcinoma is a difficult and treacherous roentgenologic diagnosis, but merely that, though in most cases characteristic signs are present, in a very small percentage of cases the findings will be deceptive and limited further by the natural pale of radiologic acumen.

WILLIAM R. STECHER, M.D.

Leukemia of the Stomach Producing Hypertrophy of the Gastric Mucosa. Leo G. Rigler. Jour. Am. Med. Assn., Dec. 19, 1936, **107,** 2025–2028.

Generalized leukemic infiltration of the viscera, as well as of the bones, is not uncommon. Involvement of the gastro-intestinal tract is repeatedly observed at autopsy. The changes produced by this disease in the stomach and in the upper part of the duodenum present a bizarre picture in the roentgenogram. There are few cases recorded in which the diagnosis was successfully made by means of roentgen examination. Two types of abnormality may be observed on roentgen examination, first, a localized infiltration, often near the pylorus, with a marked constriction of the lumen of the stomach and, second, a remarkable enlargement of the folds of mucous membrane of the stomach. Similar changes were found in the duodenum in both types of cases. The roentgen changes in the second type were interpreted as being due to an extreme grade of hypertrophic gastritis or an unusual form of multiple polyposis.

In many instances of leukemic infiltration of the gastro-intestinal tract the blood picture may be normal. This makes the diagnosis difficult.

The author reports a case in which the roentgen examination suggested this lesion in a patient formerly treated for cervical and buccal adenopathy. He made a temporary recovery under radiotherapy and died one year later. Autopsy could not be obtained. A second patient showed no response to treatment and was still living at the end of eighteen months.

CHARLES G. SUTHERLAND, M.B. (Tor.).

Chronic Gastritis. R. Schindler, M. Ortmayer, and J. F. Renshaw. Jour. Am. Med. Assn., Feb. 6, 1937, **108,** 465–468.

The diagnosis of chronic, non-specific gastritis has been obsolete for 30 years. Recent histologic and gastroscopic research have shown that chronic inflammation of the stomach is very common.

In the examination of a large group of patients with abdominal complaints 23 per cent were found to have normal stomachs, as judged by gastroscopic examination of healthy persons of all ages. About 50 per cent of the group presented mucosal changes similar to those of chronic inflammation of other mucous membranes, either layers of whitish, grayish, or greenish mucus or hyperemic spots. These lesions usually healed and the gastroscopic picture of these was designated "superficial gastritis."

Some of these showed, in later gastroscopic examinations, thin greenish gray spots that did not change in subsequent examinations. These were designated as "atrophic gastritis." This atrophic gastritis was observed without a preceding superficial gastritis, for instance, in cases of pernicious anemia. Total atrophy was also observed.

"Hypertrophic gastritis" they considered a separate clinical entity. Gastroscopically this exhibited a swollen, thickened, velvety mucous membrane, often containing hemorrhages and erosions and showing nodules or large nodes, creases, and crevasses. The course of hypertrophic gastritis is typified by failure of the mucosa to revert to normal and sudden recurrences of symptoms even while on careful management. The small erosions always heal within a week, but others may appear concurrently. No atrophy develops.

A fourth form of chronic gastritis, that of the postoperative stomach, offered the worst prognosis. All three forms of gastritis occur combined.

X-ray relief technic, which gives such splendid results in ulcer and cancer diagnosis, is disappointing in chronic gastritis.

CHARLES G. SUTHERLAND, M.B. (Tor.).

THE THYROID

Roentgen Therapy of Hyperthyroidism. P. Hess. Strahlentherapie, 1937, **58,** 74.

The author analyzes the results of roentgen therapy in hyperthyroidism in 140 patients observed during the last 10 years. He recommends doses of from 150 to 180 r per sitting. One series consists of six sittings given over a period of from two to three weeks. Two or three series may be applied at intervals of from six to eight weeks. In severe cases the single dose must usually be reduced; the total dose in this type of case should reach from 3,000 to 4,000 r. In evaluating the

results the author classified his patients under thyrotoxicosis, Basedow's struma, and true Basedow's disease. The respective percentages of cures in these groups were 40.5, 48, and 50 per cent, giving an average of 47 per cent. Improved were 37 per cent; 16 per cent had no benefit from the irradiation. It is obvious, therefore, that in Basedow's disease the results were most striking. There was no mortality in this series of patients, while on the other hand many severe cases were improved by radiation therapy.

ERNST A. POHLE, M.D., Ph.D.

TUBERCULOSIS, PULMONARY

Radiography and Tuberculosis Mortality. Franz Freund. Wien. klin. Wchnschr., Sept. 4, 1936, **49,** 1096–1098. (Reprinted by permission from British Med. Jour., Dec. 12, 1936, p. 97 of Epitome of Current Medical Literature.)

The author has been able to confirm the remarkable fact reported by other observers that a radiographic examination may reveal an advanced tuberculous lesion in persons apparently in fair health and not presenting signs of tuberculous lung infection on clinical examination. Early radiographic diagnosis followed by early treatment was responsible for a considerable decrease in the number of cases progressing toward caseation of the tuberculous infiltration.

Dr. Freund's observations are based on the investigation of 20,000 employees of the Vienna Tramways. Up to 1928 the mortality from tubercle among them was roughly the same as for the residential quarters of Vienna inhabited mainly by fairly well-to-do people. The poorer districts showed a higher mortality. But beginning with 1928 the mortality among the tramway employees dropped considerably and reached 6.5 per 1,000 (for men) in 1933, whereas the mortality from tubercle for the better classes of Vienna has not varied appreciably since 1914. The improved statistics among the tramway employees can only be explained by early radiographic examinations available to them since 1928.

Cervical Rib and Tuberculosis. Filoreto d'Agostino. Archivio di Radiologia, 1936, **12,** Nos. 3–4, 177–184.

The author found in a study of 1,110 roentgenograms, 18 cases of cervical rib, two-thirds of which were associated with frank pulmonary tuberculosis. He feels there must be some cause-effect relationship here, and offers roentgenographic findings in support of his thesis.

E. T. LEDDY, M.D.

Errors in Diagnosis of Tuberculosis, with Particular Reference to Undulant Fever. A. Behrmann. München. med. Wchnschr., Sept. 25, 1936, **39,** 1591, 1592.

A brief review of the numerous symptomatic complaints of incipient pulmonary tuberculosis are enumerated, and the author stresses the great importance of an early roentgenographic examination in all undetermined complaints which might remotely be caused by a tuberculous infection. An outline of the major nontuberculous pulmonary affections which might produce hemoptysis is presented, *viz.*, chronic bronchitis, bronchiectasis, pneumoconiosis, atelectatic process, chronic pneumonitis, lung abscess, syphilis of the lung, neoplasms, parasitic infestations, etc. Also, this symptom is commonly manifest in cardiac decompensation, and in aneurysm of the aorta, trauma, so-termed hemorrhagic diathesis, etc. It is not unusual that lymphogranuloma is considered as tuberculosis for a long period of time, even confused roentgenologically, symptomatically, and with the fever reaction (Pel-Ebstein type). Chronicity of slight elevation of temperature or subnormality is not unusual in tonsillar disease, sinusitis, middle ear disease, or chronic infections of abdominal organs (appendix) and urinary tract. Of particular note is the confusion in diagnosis in the presence of a paratyphoid infection. Recently, there has been an increase in diagnosis of Bang's disease (undulant fever), which in many respects strongly simulates incipient tuberculosis. Fortunately, the specific serologic reaction is a strong differential point. Of great importance is the confusing picture of the respective roentgenograms of early pulmonary tuberculosis and pulmonic manifestations of undulant fever. However, the degree of diffuse involvement, rapid progression, and defervescence, in the case of undulant fever, is a diagnostic aid. Clinically, the pulse rate in tuberculosis is elevated from incipiency, which is a late manifestation in Bang's disease. Both diseases show a slight degree of splenomegaly and leukopenia. The tuberculin reaction is of no great positive significance. The author concludes in suggesting an undulant fever agglutination test in any case of suggestive atypical pulmonary tuberculosis.

WILLIAM R. STECHER, M.D.